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XUM

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XUM

XUM

CONTENTS

General, physical, and inorganic

NO.		PAGE
5	The chromatography of gases and vapours. Part VI. Use of the stearates of bivalent manganese, cobalt, nickel, copper, and zinc as column liquids in gas chromatography By D. W. BARBER, C. S. G. PHILLIPS, G. F. TUSA, and A. VERDIN	18
8	Dissolution of metals and alloys. Part I. The dissolution of copper in solutions containing persulphate ion By G. C. BOND, B. M. HILL, and R. TENNISON	33
16	The nitratonitrosylruthenium complex, $RuN_2O_{7\cdot5}$ By F. S. MARTIN, J. M. FLETCHER, P. G. M. BROWN, and B. M. GATEHOUSE	76
21	Co-ordination of trimethylamine by halides of silicon, germanium, and tin By J. E. FERGUSSON, D. K. GRANT, R. H. HICKFORD, and C. J. WILKINS	99
25	Spectrophotometric determination of the acid dissociation constants of hydrogen sulphide By A. J. ELLIS and R. M. GOLDING	127
36	Hydrothermal chemistry of the silicates. Part VIII. Low-temperature crystal growth of aluminosilicates, and of some gallium and germanium analogues By R. M. BARRER, J. W. BAYNHAM, F. W. BULTITUDE, and W. M. MEIER	195
39	Solvent extraction studies. Part III. The extraction of hydrogen peroxide into tri-*n*-butyl phosphate By D. G. TUCK	218
46	Unstable intermediates. Part I. Photochemical reactions in rigid glasses By M. C. R. SYMONS and M. G. TOWNSEND	263
47	Unstable intermediates. Part II. Photolysis of hydrogen peroxide in solid alcohols: some reactions of hydroxyl radicals By J. F. GIBSON, M. C. R. SYMONS, and M. G. TOWNSEND	269
48	Unstable intermediates. Part III. Proton interaction in aliphatic free radicals By M. C. R. SYMONS	277
49	Steric hindrance in analytical chemistry. Part V. A new 2-substituted 8-hydroxyquinoline (oxine) By H. IRVING and D. J. CLIFTON	288
50	The stability of iron complexes. Part III. A comparison of 1 : 1 ferric and ferrous amino-acid complexes By D. D. PERRIN	290
52	Exchange studies of certain chelate compounds of the transitional metals. Part VI. The cobalt(II)–phenanthroline system By PETER ELLIS and R. G. WILKINS	299
54	Reactions of tin(IV) halides with ammonia derivatives. Part III. The reaction of tin(IV) halides with aliphatic amines By E. BANNISTER and G. W. A. FOWLES	310
60	Magnetochemistry. Part I. Introduction and apparatus By B. N. FIGGIS and R. S. NYHOLM	331
61	Magnetochemistry. Part II. The temperature-dependence of the magnetic susceptibility of bivalent cobalt compounds By B. N. FIGGIS and R. S. NYHOLM	338
66	Ammonolysis and aminolysis of trifluoromethyl arsenicals By W. R. CULLEN and H. J. EMELÉUS	372
67	The heptafluoropropyliodophosphines and their derivatives By H. J. EMELÉUS and J. D. SMITH	375
72	The kinetics of the hydrolysis of the chlorinated methanes By IAN FELLS and E. A. MOELWYN-HUGHES	398

XUM

NO. PAGE

76 Organic compounds of zirconium. Part VI. Reactions of zirconium tetrachloride and *iso*propoxide with fatty acids
By R. N. KAPOOR and R. C. MEHROTRA 422

77 Chemical applications of nuclear quadrupole resonance spectroscopy. Part II. Chloro-derivatives of maleic anhydride, thiophen, and anilinium salts
By M. J. S. DEWAR and E. A. C. LUCKEN 426

78 Peroxides of elements other than carbon. Part III. The formation of boron peroxides by autoxidation
By M. H. ABRAHAM and ALWYN G. DAVIES 429

79 Peroxides of elements other than carbon. Part IV. The autoxidation of tri-*sec.*-butylboron to *sec.*-butyldi-(*sec.*-butylperoxy)boron
By ALWYN G. DAVIES and D. G. HARE 438

NOTES

85 Structure of fulminate ion
By KARTAR SINGH 459

92 Thermodynamics of the hydrogen- and hydroxy-complexes of aluminium with ethylenediaminetetra-acetic acid
By T. RANDALL and L. A. K. STAVELEY 472

Physical organic

7 Spectrophotometry in the far-ultraviolet region. Part II. Absorption spectra of steroids and triterpenoids
By D. W. TURNER 30

10 Anionotropic systems. Part VII. Reversible rearrangements of the 1-naphthyl-3-phenylallyl alcohols. A kinetic determination of the conjugation energies of the α- and β-vinylnaphthalene systems
By (the late) E. A. BRAUDE and P. H. GORE 41

14 An examination of some approximations in antisymmetrized molecular-orbital calculations
By E. THEAL STEWART 70

22 Kinetic salt effects and mechanism in the hydrolysis of positively charged esters
By G. AKSNES and J. E. PRUE 103

23 Kinetic salt effects on the reaction between persulphate and iodide ions
By A. INDELLI and J. E. PRUE 107

33 Physical properties of anthraquinone and its derivatives. Part I. Infrared spectra
By H. BLOOM, L. H. BRIGGS, and B. CLEVERLEY 178

43 Interaction of Lewis acids with aromatic hydrocarbons and bases. Part XVIII. Aromatic hydrocarbon picrates in chloroform
By R. FOSTER, D. LL. HAMMICK, and S. F. PEARCE 244

51 The effect of acid on the electronic spectra of organic molecules contanining conjugated and unconjugated nitrogen atoms
By J. N. MURRELL 296

53 Hydrolysis of dialkylphosphinic fluorides and dialkyl phosphorofluoridates. Kinetic and tracer studies
By M. HALMANN 305

55 Acetyl chloride as a polar solvent. Part I. Solubility of substances and formation of solvates in acetyl chloride
By RAM CHAND PAUL, DULA SINGH, and SARJIT SINGH SANDHU 315

56 Acetyl chloride as a polar solvent. Part II. Solvolytic reactions in acetyl chloride
By RAM CHAND PAUL, DULA SINGH, and SARJIT SINGH SANDHU 319

57 Acetyl chloride as a polar solvent. Part III. Formation of acid–base neutralization complexes in acetyl chloride
By (MISS) KAMLA GOYAL, RAM CHAND PAUL, and SARJIT SINGH SANDHU . . 322

58 Acetyl chloride as a polar solvent. Part IV. Conductometric titrations in acetyl chloride
By BALDEV SINGH MANHAS, RAM CHAND PAUL, and SARJIT SINGH SANDHU . . 325

NO. PAGE

80 Synthetical applications of activated metal catalysts. Part VI. Desulphurisations with Raney cobalt
By G. M. BADGER, N. KOWANKO, and W. H. F. SASSE 440

NOTES

87 Steric effects and hydrogen isotope exchange in 1 : 2 : 3-trimethoxybenzene
By D. P. N. SATCHELL 463

94 Nuclear magnetic resonance of *cis-trans*-β-methylmuconic acid
By J. A. ELVIDGE 474

Organic

1 Triazaphenanthrenes. Part III. Synthesis of some 9-aryl-2 : 3 : 10-triazaphenanthrenes
By C. M. ATKINSON and R. E. RODWAY 1

2 Triazaphenanthrenes. Part IV. Some 9-aryl-3-methyl-1 : 2 : 10-triazaphenanthrenes
By C. M. ATKINSON and R. E. RODWAY 6

3 The chemical effects of γ-radiation on organic systems. Part III. The action of radiation on triethylamine alone or mixed with bromobenzene
By G. A. SWAN, P. S. TIMMONS, and D. WRIGHT 9

4 Polyfluoroarenes. Part I. Pentafluorophenol
By J. M. BIRCHALL and R. N. HASZELDINE 13

6 Allenes. Part II. Reactions of prop-2-yn-1-ols with thionyl chloride
By Y. R. BHATIA, PHYLLIS D. LANDOR, and S. R. LANDOR 24

9 Oxygen heterocycles. Part IX. The Elbs reaction in the dibenzofuran series
By NG. PH. BUU-HOÏ and DENISE LAVIT 38

11 Purines, pyrimidines, and glyoxalines. Part XI. Some oxazolidino- and thiazolidino-[2 : 3-*a*]pyrimidines, and a synthesis of thymidine
By G. SHAW and R. N. WARRENER 50

12 *pseudo*Azulenes. Part II. A tricyclic *cyclo*penta[*b*]thiapyran and some nitrogen analogues
By G. V. BOYD 55

13 The abnormal hydrolysis of methyl β-methylthio- and 3-ethylthio-propionate
By FREDERICK CHALLENGER and HARRY D. HOLLINGWORTH 61

15 Triterpene constituents of the fruits of the osage orange (*Maclura pomifera*)
By K. G. LEWIS 73

17 Amino-acids and peptides. Part II. The constitution of hypoglycin A
By E. V. ELLINGTON, C. H. HASSALL, J. R. PLIMMER, and C. E. SEAFORTH . . 80

18 Cardenolides. Part III. The constitution of calotropagenin
By C. H. HASSALL and (the late) K. REYLE 85

19 Cyto-active amino-acids and peptides. Part V. Derivatives of *p*-amino- and *p*-mercapto-phenylalanine
By F. BERGEL and J. A. STOCK 90

20 Cyto-active amino-acids and peptides. Part VI. Synthesis of *N'*-α-aminoacyl-*NN*-di-(2-chloroethyl)-*p*-phenylenediamines
By F. BERGEL and J. A. STOCK 97

24 A general stereoselective synthesis of olefins
By J. W. CORNFORTH, (MRS.) R. H. CORNFORTH, and K. K. MATHEW . . . 112

26 Picrotoxin and tutin. Part IX
By R. M. CARMAN, GHULAM HASSAN, and R. B. JOHNS 130

27 Stereochemical investigations of cyclic bases. Part IV. Hofmann degradation of 6α- and 6β-cholestanyltrimethylammonium salts
By B. B. GENT and J. MCKENNA 137

28 The electronic interaction between benzenoid rings in condensed aromatic hydrocarbons. 1 : 12-2 : 3-4 : 5-6 : 7-8 : 9-10 : 11-Hexabenzocoronene, 1 : 2-3 : 4-5 : 6-10 : 11-tetrabenzoanthanthrene, and 4 : 5-6 : 7-11 : 12-13 : 14-tetrabenzoperopyrene
By E. CLAR, C. T. IRONSIDE, and M. ZANDER 142

XUM

NO.		PAGE
29	Fluoro*cyclo*hexanes. Part IV. 1*H* : 2*H*/4*H*- and 1*H* : 2*H* : 4H/-Nonafluoro*cyclo*-hexane and related compounds By R. STEPHENS, J. C. TATLOW, and E. H. WISEMAN	148
30	Fluoro*cyclo*hexanes. Part V. 1*H* : 4*H*/2*H* : 5*H*-, 1*H* : 5*H*/2*H* : 4*H*-, 1*H* : 2*H*/-4*H* : 5*H*-, and 1*H* : 2*H* : 4*H*/5*H*-Octafluoro*cyclo*hexane and derived compounds By E. NIELD, R. STEPHENS, and J. C. TATLOW	159
31	Aromatic polyfluoro-compounds. Part I. The synthesis of aromatic polyfluoro-compounds from pentafluorobenzene By E. NIELD, R. STEPHENS, and J. C. TATLOW	166
32	Phenolic alkaloids occurring in *Lycoris radiata* By SHOJIRO UYEO and NOBORU YANAIHARA	172
34	Pyrroles and related compounds. Part II. Michael addition to pyrromethenes By A. C. IAIN and G. W. KENNER	185
35	The preparation and rearrangement of benzoates and substituted benzoates of di-bromopropanols By J. H. C. NAYLER	189
37	Heterocyclic imines and amines. Part IX. Glutarimidine and the imidine from α-phenylglutaronitrile By J. A. ELVIDGE, R. P. LINSTEAD, and ANN M. SALAMAN	208
38	Triterpenoids. Part LVII. The oxidation of norfriedelanone with selenium dioxide By GEORGE BROWNLIE, F. S. SPRING, and ROBERT STEVENSON	216
40	Aspects of stereochemistry. Part XI. Epoxide formation in the *cyclo*hexene and *bicyclo*heptene series By H. B. HENBEST and B. NICHOLLS	221
41	Aspects of stereochemistry. Part XII. A specific directing effect in the mercuration of some 4-substituted *cyclo*hexenes and *cis*-hex-3-enol By H. B. HENBEST and B. NICHOLLS	227
42	Studies on the Diels–Alder reaction. Part V. Further transformation products of *cis-syn*-1 : 2 : 3 : 4 : 5 : 6 : 12 : 13 : 14 : 15-decahydro-8-methoxy-1 : 4-dioxochrysene By P. A. ROBINS and JAMES WALKER	237
44	Reactions of 1 : 2-dichloro-3 : 4-epoxybutane and related compounds By E. G. E. HAWKINS	248
45	The direct introduction of the diazonium group into aromatic nuclei. Part V. The action of buffered nitrous acid on aromatic hydroxy-acids By J. M. TEDDER and G. THEAKER	257
59	Reduced cyclic compounds. Part VII. A new route to 2-substituted *cyclo*pent-2-enones By M. F. ANSELL and J. W. DUCKER	329
62	Steroids and Walden inversion. Part XLI. The deamination of some A-nor-, B-nor, and 17-amino-steroids By C. W. SHOPPEE and J. C. P. SLY	345
63	Phospholipids. Part IV. *myo*Inositol 2-phosphate By D. M. BROWN and G. E. HALL	357
64	Reaction of amino-derivatives of anthraquinone, fluorenone, and fluorene with nitrobenzene and α-nitronaphthalene By WILLIAM BRADLEY and F. P. WILLIAMS	360
65	Synthesis in the santonin series. Part IV. A synthesis of the 7α(*H*)-3-oxoeudesm-4-en-12-oic and 7β(*H*)-3-oxoeudesm-4-en-12-oic acids based on a method of oxidation of a methylene to a carboxyl group By R. HOWE, F. J. MCQUILLIN, and R. W. TEMPLE	363
68	A quantitative study of the arylation of naphthalene by means of diazonium salts and zinc By B. A. MARSHALL and WILLIAM A. WATERS	381
69	Partial synthesis of vitamins D_2 and D_3 By H. H. INHOFFEN, K. IRMSCHER, H. HIRSCHFELD, U. STACHE, and A. KREUTZER	385
70	Oxidation of polyhalogeno-compounds. Part II. Photolysis and photochemical oxidation of some chlorofluoroethanes By R. N. HASZELDINE and F. NYMAN	387

XUM

NO.		PAGE
71	Thiohydantoins. Part V. A new synthesis of 5 : 5-disubstituted 4-thiohydantoins By H. C. Carrington, C. H. Vasey, and W. S. Waring	396
73	The synthesis of 1-glycosylbenziminazoles By A. J. Cleaver, A. B. Foster, and W. G. Overend	409
74	Some dichloro- and dibromo-derivatives of 1 : 2 : 3 : 4-tetrahydrophenazine and *cis*-1 : 2 : 3 : 4 : 5 : 10 : 11 : 12-octahydrophenazine By Ruth M. Scott and Muriel Tomlinson	417
75	Oxidation of polyhalogeno-compounds. Part III. Thermal oxidation of some chlorofluoroethanes By R. N. Haszeldine and F. Nyman	420
81	The reaction between diphenylamine and malonic esters By R. E. Bowman, A. Campbell, and (Miss) E. M. Tanner	444
82	Organic nitrates. Part II. 9-Fluorenyl nitrate By G. W. H. Cheeseman	448
83	Organic nitrates. Part III. Triphenylmethyl nitrate and 9-phenyl-9-fluorenyl nitrate By G. W. H. Cheeseman	452

Notes

84	Some reactions of xanthhydryl chloride By G. W. H. Cheeseman	458
86	The rearrangement of nitrones By A. H. Wragg and T. S. Stevens	461
88	Alicyclic studies. Part XIV. An improved synthesis of 3 : 4-5 : 6-dibenzophenanthrene and 1 : 12-benzoperylene By Yanina Altman and David Ginsburg	466
89	The extractives of *Dysoxylum spectabile*, Hook By R. C. Cambie	468
90	Chemistry of the *Coprosma* genus. Part XI. The colouring matters from *Coprosma foetidissima* By E. G. Brooker	470
91	Allylic rearrangement of an αβ-unsaturated hydroperoxide By B. Lythgoe and S. Trippett	471
93	Synthesis of 5-bromotryptophan and some derivatives By D. G. Harvey	473
95	Preparation of symmetrically substituted deoxybenzoins By P. H. Carter, J. Cymerman Craig, (Miss) Ruth E. Lack, and M. Moyle	476
96	The action of thionyl chloride on 2-methyl- and 2-ethyl-1 : 3-dioxolan-2-carboxylic acid By R. P. A. Sneeden	477
97	Preparation of 17α-acetoxy-6α-methylprogesterone By (Miss) S. P. Barton, B. Ellis, and V. Petrow	478
98	11-Ethoxy-1 : 2 : 3 : 4 : 10 : 11-hexahydrofluoren-1-one. A correction By F. H. Howell and D. A. H. Taylor	480

INDEX OF AUTHORS' NAMES

ABRAHAM, M. H., and Davies, Alwyn G., 429
Aksnes, G., and Prue, J. E., 103
Altman, Y., and Ginsburg, D., 466
Ansell, M. F., and Ducker, J. W., 329
Atkinson, C. M., and Rodway, R. E., 1, 6
Badger, G. M., Kowanko, N., and Sasse, W. H. F., 440
Bannister, E., and Fowles, G. W. A., 310
Barber, D. W., Phillips, C. S. G., Tusa, G. F., and Verdin, A., 18
Barrer, R. M., Baynham, J. W., Bultitude, F. W., and Meier, W. M., 195
Barton, S. P., Ellis, B., and Petrow, V., 478
Baynham, J. W. See Barrer, R. M., 195
Bergel, F., and Stock, J. A., 90, 97
Bhatia, Y. R., Landor, P. D., and Landor, S. R., 24
Birchall, J. M., and Haszeldine, R. N., 13
Bloom, H., Briggs, L. H., and Cleverley, B., 178
Bond, G. C., Hill, B. M., and Tennison, R., 33
Bowman, R. E., Campbell, A., and Tanner, E. M., 444
Boyd, G. V., 55
Bradley, W., and Williams, F. P., 360
Braude, E. A., and Gore, P. H., 41
Briggs, L. H. See Bloom, H., 178
Brooker, E. G., 470
Brown, D. M., and Hall, G. E., 357
Brown, P. G. M. See Martin, F. S., 76
Brownlie, G., Spring, F. S., and Stevenson, R., 216
Bultitude, F. W. See Barrer, R. M., 195
Buu-Hoï, Ng. Ph., and Lavit, D., 38
Cambie, R. C., 468
Campbell, A. See Bowman, R. E., 444
Carman, R. M., Hassan, G., and Johns, R. B., 130
Carrington, H. C., Vasey, C. H., and Waring, W. S., 396
Carter, P. H., Cymerman-Craig, J., Lack, R. E., and Moyle, M., 476
Challenger, F., and Hollingworth, H. D., 61
Cheeseman, G. W. H., 448, 452, 458
Clar, E., Ironside, C. T., and Zander, M., 142
Cleaver, A. J., Foster, A. B., and Overend, W. G., 409
Cleverley, B. See Bloom, H., 178
Clifton, D. J. See Irving, H., 288
Cornforth, J. W., Cornforth, R. H., and Mathew, K. K., 112
Cornforth, R. H. See Cornforth, J. W., 112
Cullen, W. R., and Emeléus, H. J., 372
Cymerman-Craig, J. See Carter, P. H., 476
Davies, Alwyn G., and Hare, D. G., 438
Davies, Alwyn G. See also Abraham, M. H., 429
Dewar, M. J. S., and Lucken, E. A. C., 426
Ducker, J. W. See Ansell, M. F., 329
Ellington, E. V., Hassall, C. H., Plimmer, J. R., and Seaforth, C. E., 80
Ellis, A. J., and Golding, R. M., 127
Ellis, B. See Barton, S. P., 478
Ellis, P., and Wilkins, R. G., 299
Elvidge, J. A., 474
Elvidge, J. A., Linstead, R. P., and Salaman, A. M., 208
Emeléus, H. J., and Smith, J. D., 375
Emeléus, H. J. See also Cullen, W. R., 372
Fells, I., and Moelwyn-Hughes, E. A., 398
Fergusson, J. E., Grant, D. K., Hickford, R. H., and Wilkins, C. J., 99
Figgis, B. N., and Nyholm, R. S., 331, 338
Fletcher, J. M. See Martin, F. S., 76
Foster, A. B. See Cleaver, A. J., 409
Foster, R., Hammick, D. Ll., and Pearce, S. F., 244
Fowles, G. W. A. See Bannister, E., 310
Gatehouse, B. M. See Martin, F. S., 76
Gent, B. B., and McKenna, J., 137
Gibson, J. F., Symons, M. C. R., and Townsend, M. G., 269
Ginsburg, D. See Altman, Y., 466
Golding, R. M. See Ellis, A. J., 127
Gore, P. H. See Braude, E. A., 41
Goyal, K., Paul, R. C., and Sandhu, S. S., 322
Grant, D. K. See Fergusson, J. E., 99
Hall, G. E. See Brown, D. M., 357
Halmann, M., 305
Hammick, D. Ll. See Foster, R., 244
Hare, D. G. See Davies, Alwyn G., 438
Harvey, D. G., 473
Hassall, C. H., and Reyle, K., 85
Hassall, C. H. See also Ellington, E. V., 80
Hassan, G. See Carman, R. M., 130
Haszeldine, R. N., and Nyman, F., 387, 420
Haszeldine, R. N. See Birchall, J. M., 13
Hawkins, E. G. E., 248
Henbest, H. B., and Nicholls, B., 221, 227
Hickford, R. H. See Fergusson, J. E., 99
Hill, B. M. See Bond, G. C., 33
Hirschfeld, H. See Inhoffen, H. H., 385
Hollingworth, H. D. See Challenger, F., 61
Howe, R., McQuillin, F. J., and Temple, R. W., 363
Howell, F. H., and Taylor, D. A. H., 480
Indelli, A., and Prue, J. E., 107
Inhoffen, H. H., Irmscher, K., Hirschfeld, H., Stache, U., and Kreutzer, A., 385
Irmscher, K. See Inhoffen, H. H., 385
Ironside, C. T. See Clar, E., 142
Irving, H., and Clifton, D. J., 288
Jain, A. C., and Kenner, G. W., 185
Johns, R. B. See Carman, R. M., 130
Kapoor, R. N., and Mehrotra, R. C., 422
Kenner, G. W. See Jain, A. C., 185
Kowanko, N. See Badger, G. M., 440
Kreutzer, A. See Inhoffen, H. H., 385
Lack, R. E. See Carter, P. H., 476
Landor, P. D. See Bhatia, Y. R., 24
Landor, S. R. See Bhatia, Y. R., 24
Lavit, D. See Buu-Hoï, Ng. Ph., 38
Lewis, K. G., 73
Linstead, R. P. See Elvidge, J. A., 208
Lucken, E. A. C. See Dewar, M. J. S., 426
Lythgoe, B., and Trippett, S., 471
McKenna, J. See Gent, B. B., 137
McQuillin, F. J. See Howe, R., 363
Manhas, B. S., Paul, R. C., and Sandhu, S. S., 325
Marshall, B. A., and Waters, W. A., 381
Martin, F. S., Fletcher, J. M., Brown, P. G. M., and Gatehouse, B. M., 76
Mathew, K. K. See Cornforth, J. W., 112
Mehrotra, R. C. See Kapoor, R. N., 422
Meier, W. M. See Barrer, R. M., 195
Moelwyn-Hughes, E. A. See Fells, I., 398
Moyle, M. See Carter, P. H., 476
Murrell, J. N., 296
Nayler, J. H. C., 189
Nicholls, B. See Henbest, H. B., 221, 227

Nield, E., Stephens, R., and Tatlow, J. C., 159, 166
Nyholm, R. S. See Figgis, B. N., 331, 338
Nyman, F. See Haszeldine, R. N., 387, 420
Overend, W. G. See Cleaver, A. J., 409
Paul, R. C., Singh, D., and Sandhu, S. S., 315, 319
Paul, R. C. See also Goyal, K., 322, and Manhas, B. S., 325
Pearce, S. F. See Foster, R., 244
Perrin, D. D., 290
Petrow, V. See Barton, S. P., 478
Phillips, C. S. G. See Barber, D. W., 18
Plimmer, J. R. See Ellington, J. R., 80
Prue, J. E. See Aksnes, G., 103, and Indelli, A., 107
Randall, T., and Staveley, L. A. K., 472
Reyle, K. See Hassall, C. H., 85
Robins, P. A., and Walker, J., 237
Rodway, R. E. See Atkinson, C. M., 1, 6
Salaman, A. M. See Elvidge, J. A., 208
Sandhu, S. S. See Goyal, K., 322, Manhas, B. S., 325, and Paul, R. C., 315, 319
Sasse, W. H. F. See Badger, G. M., 440
Satchell, D. P. N., 463
Scott, R. M., and Tomlinson, M., 417
Seaforth, C. E. See Ellington, E. V., 80
Shaw, G., and Warrener, R. N., 50
Shoppee, C. W., and Sly, J. C. P., 345
Singh, D. See Goyal, K., 322, and Paul, R. C., 315, 319
Singh, K., 459
Sly, J. C. P. See Shoppee, C. W., 345
Smith, J. D. See Emeléus, H. J., 375
Sneeden, R. P. A., 477
Spring, F. S. See Brownlie, G., 216
Stache, U. See Inhoffen, H. H., 385
Staveley, L. A. K. See Randall, T., 472
Stephens, R., Tatlow, J. C., and Wiseman, E. H., 148
Stephens, R. See also Nield, E., 159, 166
Stevens, T. S. See Wragg, A. H., 461
Stevenson, R. See Brownlie, G., 216
Stewart, E. T., 70
Stock, J. A. See Bergel, F., 90, 97
Swan, G. A., Timmons, P. S., and Wright, D., 9
Symons, M. C. R., 277
Symons, M. C. R., and Townsend, M. G., 263
Symons, M. C. R. See also Gibson, J. F., 269
Tanner, E. M. See Bowman, R. E., 444
Tatlow, J. C. See Nield, E., 159, 166, and Stephens, R., 148
Taylor, D. A. H. See Howell, F. H., 480
Tedder, J. M., and Theaker, G., 257
Temple, R. W. See Howe, R., 363
Tennison, R. See Bond, G. C., 33
Theaker, G. See Tedder, J. M., 257
Timmons, P. S. See Swan, G. A., 9
Tomlinson, M. See Scott, R. M., 417
Townsend, M. G. See Gibson, J. F., 269, and Symons, M. C. R., 263
Trippett, S. See Lythgoe, B., 471
Tuck, D. G., 218
Turner, D. W., 30
Tusa, G. F. See Barber, D. W., 18
Uyeo, S., and Yanaihara, N., 172
Vasey, C. H. See Carrington, H. C., 396
Verdin, A. See Barber, D. W., 18
Walker, J. See Robins, P. A., 237
Waring, W. S. See Carrington, H. C., 396
Warrener, R. N. See Shaw, G., 50
Waters, W. A. See Marshall, B. A., 381
Wilkins, C. J. See Fergusson, J. E., 99
Wilkins, R. G. See Ellis, P., 299
Williams, F. P. See Bradley, W., 360
Wiseman, E. H. See Stephens, R., 148
Wragg, A. H., and Stevens, T. S., 461
Wright, D. See Swan, G. A., 9
Yanaihara, N. See Uyeo, S., 172
Zander, M. See Clar, E., 142

XUM

PAPERS ACCEPTED

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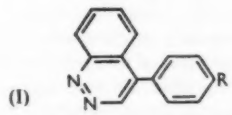
1. *Triazaphenanthrenes. Part III.*[1] *Synthesis of Some 9-Aryl-2 : 3 : 10-triazaphenanthrenes.*

By C. M. Atkinson and R. E. Rodway.

Cyclodehydration of the phenylpyridazines (II; R′ = NH·COAr) to 2 : 3 : 10-triazaphenanthrenes (III) is best effected with phosphorus pentoxide in nitrobenzene. The presence of a nitro-substituent prevents cyclisation in some instances. Methiodides of the triazaphenanthrenes were biologically inactive.

Of the twenty-eight possible triazaphenanthrene systems, derivatives of only five have been described. 1 : 3 : 9-Triazaphenanthrenes have been prepared[2,3] and the 1 : 2 : 9-system was described in Part II.[1] Two isolated 1 : 5 : 9- and 1 : 5 : 10-triazaphenanthrenes have been obtained as by-products in the synthesis of 2′ : 3-diamino-2 : 3′-dipyridyl from the corresponding diamide.[4] The synthesis of some 2 : 3 : 10-triazaphenanthrenes from 4-arylcinnolines (I) is now described.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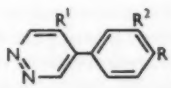
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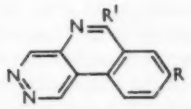
(III)

One of the key intermediates, 4-phenylcinnoline (I; R = H), was prepared[5] from *o*-aminobenzophenone which was available more readily on a large scale from *o*-benzoylbenzamide[6] than from toluene-*p*-sulphonylanthranilic acid.[7] Oxidation of the cinnoline (I; R = H) to 5-phenylpyridazine-3 : 4-dicarboxylic acid and subsequent decarboxylation in 2-ethoxyethanol provided a cleaner sample of the monoacid (II; R = R^2 = H, R^1 = CO_2H), m. p. 220° (decomp.), than that obtained by the literature method;[5] Stoermer and Fincke were in error in assigning this melting point to the dicarboxylic acid. Attempts to convert the monoacid into the amide (II; R = R^2 = H, R^1 = $CO{\cdot}NH_2$) *via* the acid chloride were unsuccessful, possibly because of cyclisation to the corresponding diazafluorenone.[8] However, the methyl ester gave the amide readily, from which the amine (II; R = R^2 = H, R^1 = NH_2) was obtained by treatment with potassium hypobromite. An attempt to prepare this amine directly from the monoacid by using hydroxylamine hydrochloride in polyphosphoric acid[9] failed.

[1] Part II, Atkinson and Mattocks, *J.*, 1957, 3722.
[2] Galland and Robinson, *J.*, 1925, **127**, 1493.
[3] Atkinson and Mattocks, *J.*, 1957, 3718.
[4] Brydowna, *Roczniki Chem.*, 1934, **14**, 304.
[5] Stoermer and Fincke, *Ber.*, 1909, **42**, 3115.
[6] Hewett, Lermit, Openshaw, Todd, Williams, and Woodward, *J.*, 1948, 292.
[7] Scheifile and De Tar, *Org. Synth.*, **32**, 8.
[8] Rule and Bretscher, *J.*, 1927, 925; Bretscher, Rule, and Spence, *J.*, 1928, 1493; Bell, *J.*, 1928, 3247.
[9] Snyder, *J. Amer. Chem. Soc.*, 1953, **75**, 2014.

XUM

Cyclodehydration of the benzamido-derivative (II; R = R^2 = H, R^1 = NHBz) was not readily achieved; thus, heating under reflux with phosphorus oxychloride alone [10] or mixed with nitrobenzene,[11] or with the further addition of stannic chloride [12] had no effect. The use of phosphorus pentoxide in boiling toluene or tetralin [13,14] gave similar results, but in nitrobenzene 9-phenyl-2 : 3 : 10-triazaphenanthrene (III; R = H, R^1 = Ph) was formed in yields of about 50%. Phosphorus pentoxide alone [14] gave no useful product, and although admixture with polyphosphoric acid [15] provided some (20%) of the triazaphenanthrene, difficulties in isolation discouraged variations of this method. An optimum yield of about 26% was obtained by cyclisation in a melt of aluminium chloride–sodium chloride,[16] so this, too, was discarded in favour of phosphorus pentoxide in nitrobenzene.

4-Amino-5-phenylpyridazine (II; R = R^2 = H, R^1 = NH_2) was readily converted into the *o*-, *m*-, and *p*-nitrobenzoyl derivatives, the last two of which were cyclised to the corresponding triazaphenanthrenes. The *o*-nitrobenzamido-derivative resisted cyclisation, and comparison with the preceding results suggests that steric factors are responsible; this is supported by Walls' failure [17] to prepare 7-nitro-9-*o*-nitrophenylphenanthridine and by his isolation of only a small yield of the 3-nitro-analogue.

Quaternisation of 9-*p*-nitrophenyl-2 : 3 : 10-triazaphenanthrene (III; R = H, R^1 = *p*-NO_2·C_6H_4) with dimethyl sulphate gave a mixture from which one pure monomethiodide was isolated. Reduction before quaternisation yielded a 9-*p*-aminophenyl-2 : 3 : 10-triazaphenanthrene monomethiodide, but in the *m*-aminophenyl series, no pure salt was isolated from treatment with methyl iodide in nitromethane. Reaction of 9-phenyl-2 : 3 : 10-triazaphenanthrene (III; R = H, R^1 = Ph) with methyl iodide yielded a monomethiodide, but attempts to form a diquaternary derivative failed.

A similar scheme from 4-*p*-methoxyphenylcinnoline (I; R = OMe) [18] was planned, but a derived triazaphenanthrene could not be synthesised. The methoxy-cinnoline (I; R = OMe) was oxidised to 5-*p*-methoxyphenylpyridazine-3 : 4-dicarboxylic acid as described by Stoermer and Gaus [18] who attributed to this acid the melting point which we found for the monocarboxylic acid (II; R = OMe, R^1 = CO_2H, R^2 = H). The diacid was best decarboxylated in 2-ethoxyethanol, the literature method giving only unchanged material; dry heating or decarboxylation in diethylene glycol gave a lower yield of less pure material. Nitration of the monoacid gave the *Bz*-nitro-derivative (II; R = OMe, R^1 = CO_2H, R^2 = NO_2), represented thus in view of the stability towards nitration of other pyridazine acids lacking the phenyl substituent [18] and the directive properties of the other groups present. Its amide was converted into the amine (II; R = OMe, R^1 = NH_2, R^2 = NO_2), a direct method from the acid and hydroxylamine [9] being unsuccessful. The benzamido-compound (II; R = OMe, R^1 = NHBz, R^2 = NO_2) could not be cyclised; this behaviour was not unexpected in view of the known deactivating effect of a nitro-group, especially *ortho* or *para* to the point at which ring-closure might occur.[10b] Replacement of the nitro-group by the ethoxycarbonylamino-group would probably overcome this,[19] but because of difficulties encountered in the reduction of the nitro-group only the compound (II; R = OMe, R^1 = NHBz, R^2 = NH_2) has been prepared.

Pure 9-*p*-aminophenyl-2 : 3 : 10-triazaphenanthrene monomethiodide and crude 9-*p*-nitro- and 9-*m*-nitro-phenyl-2 : 3 : 10-triazaphenanthrene methiodide are ineffective against

[10] (*a*) Morgan and Walls, *J.*, 1931, 2447; Walls, *J.*, 1934, 104; (*b*) Ritchie, *J. Proc. Roy. Soc. N.S.W.*, 1945, **78**, 147.
[11] Walls, *J. Soc. Chem. Ind.*, 1947, **66**, 182; *J.*, 1945, 294.
[12] Barber, Bretherick, Eldridge, Holt, and Wragg, *J. Soc. Chem. Ind.*, 1950, **69**, 82; Petrow and Wragg, *J.*, 1950, 3516; Nunn, Schofield, and Theobald, *J.*, 1952, 2797.
[13] Bischler and Napieralski, *Ber.*, 1893, **26**, 1903; Ritchie, *J. Proc. Roy. Soc. N.S.W.*, 1945, **78**, 134.
[14] Petrow, Stack, and Wragg, *J.*, 1943, 316.
[15] Taylor and Kalenda, *J. Amer. Chem. Soc.*, 1954, **76**, 1699; Badger and Sasse, *J.*, 1957, 4.
[16] Ebel, G.P. 614,196/1935: *Chem. Abs.*, 1935, **29**, 5859.
[17] Walls, *J.*, 1932, 2225.
[18] Stoermer and Gaus, *Ber.*, 1912, **45**, 3104.
[19] Walls, *J.*, 1947, 67.

P. berghei, *B. rodhaini*, *T. congolense*, *T. equiperdum*, and *T. cruzi* in mice; they were active against hæmolytic *Streptococcus*, *Staph. aureus*, *B. coli*, and *Candida albicans* only at concentrations of about 50 mg. % when tested in Hedley Wright broth.

Experimental

5-Phenylpyridazine-3 : 4-dicarboxylic Acid.—Hot aqueous potassium permanganate (200 g. in 2 l.) was added dropwise (*ca.* 3 hr.) with stirring to a suspension of 4-phenylcinnoline (40 g.) in water (3 l.) at *ca.* 90° and heating and stirring were then continued for a further hour. The excess of permanganate was destroyed by alcohol, and the manganese dioxide digested with hot water (*ca.* 300 c.c.). The filtrate and washings were combined and concentrated to *ca.* 800 c.c., cooled, and acidified with a large excess of dilute sulphuric acid to yield a pale yellow solid (44·4 g.), m. p. 148—150° (efferv.) [remelting at 214° (decomp.)].

5-Phenylpyridazine-4-carboxylic Acid.—The crude foregoing acid (40 g.) and ethyl 2-hydroxyethyl ether (120 c.c.) were heated to boiling in an oil-bath during *ca.* 15 min. Heating was continued until evolution of gas had almost ceased (3—4 min.), then the mixture was removed from the bath, allowed to cool, and filtered; the residue was washed with a small volume of alcohol and the crude mono-acid twice crystallised from methanol (charcoal), giving cubes of 5-phenylpyridazine-4-carboxylic acid (16—18 g., 46—51% based on 4-phenylcinnoline), m. p. 222—224° (decomp.) (Stoermer and Fincke [5] give m. p. 220—221°, decomp.) (Found: C, 66·2; H, 4·1; N, 15·0. Calc. for $C_{11}H_8O_2N_2$: C, 66·0; H, 4·0; N, 14·0%).

Methyl 5-Phenylpyridazine-4-carboxylate.—A solution of diazomethane in dioxan (*ca.* 400 c.c.; from 40 g. of *N*-methylnitrosourea) was added dropwise with stirring during 45 min. to a suspension of the powdered carboxylic acid [40 g.; m. p. 220—222° (decomp.)] in dioxan (1·5 l.) and stirring was continued until dissolution was complete (*ca.* 15 min.). Next day the clarified solution was concentrated under reduced pressure to *ca.* 120 c.c. on the steam-bath and poured into ice and water (*ca.* 1·2 l.). The crude *ester* on recrystallisation (charcoal) from light petroleum (b. p. 90—110°) formed needles (34·4 g., 80%), m. p. 103—105° (Found: C, 66·9; H, 4·8; N, 13·3. $C_{12}H_{10}O_2N_2$ requires C, 67·3; H, 4·7; N, 13·1%).

4-Carbamoyl-5-phenylpyridazine.—Powdered methyl 5-phenylpyridazine-4-carboxylate (20 g.) and methanolic ammonia (*ca.* 1 l.) [prepared by saturating methanol (1 l.) with dry ammonia (*ca.* 59 g.) in an ice bath] were kept at room temperature for 8 days. Removal of the solvent and storage in a vacuum desiccator gave the crude amide, which was purified by concentrating a chloroform (*ca.* 800 c.c.) solution; drying at 100° gave dull blades of *4-carbamoyl-5-phenylpyridazine* (16·3 g., 88%), m. p. 170—172° (Found: C, 66·2; H, 4·6; N, 21·3. $C_{11}H_9ON_3$ requires C, 66·3; H, 4·55; N, 21·1%).

4-Amino-5-phenylpyridazine.—Powdered 4-carbamoyl-5-phenylpyridazine (26 g.) was added in one portion to aqueous potassium hypobromite [370 c.c., from bromine (8·0 c.c.), potassium hydroxide (40 g.), and water (400 c.c.) at 0°] and stirred at 0° for 45 min. To this solution was added more aqueous potassium hydroxide (220 c.c., 10%), and the mixture was heated at 80° for 35 min. Cooling and crystallisation of the crude amine from water (charcoal) yielded long blades (18·0 g., 80%), m. p. 153—155°. Recrystallisation from benzene gave the pure *amine* as thick pale yellow blades, m. p. 154—156° (Found: C, 70·0; H, 5·2; N, 24·8. $C_{10}H_9N_3$ requires C, 70·15; H, 5·3; N, 24·55%).

4-Benzamido-5-phenylpyridazine.—4-Amino-5-phenylpyridazine was benzoylated with benzoyl chloride in pyridine on the steam bath for 3 hr. *4-Benzamido-5-phenylpyridazine* (88%) formed plates (from alcohol), m. p. 202—204° (Found: C, 73·7; H, 4·6; N, 15·65. $C_{17}H_{13}ON_3$ requires C, 74·2; H, 4·8; N, 15·3%).

9-Phenyl-2 : 3 : 10-triazaphenanthrene.—Phosphorus pentoxide (*ca.* 4·8 g.) was added to a solution of 4-benzamido-5-phenylpyridazine (2·4 g.) in dry nitrobenzene (48 c.c.) at *ca.* 130° and the mixture stirred at *ca.* 180° for 6 hr., with a further addition of phosphorus pentoxide (*ca.* 2·4 g.) after 3 hr. After cooling, water was added and nitrobenzene removed in steam. The aqueous residue was filtered hot and the filtrate made alkaline with dilute sodium hydroxide solution. The precipitate (1·7 g.) crystallised from aqueous acetone (charcoal) as dark yellow blades (1·2 g., 53%), m. p. 193—195°. Pure *9-phenyl-2 : 3 : 10-triazaphenanthrene* had m. p. 196—198° (from methanol) (Found: C, 79·2; H, 4·3; N, 16·4. $C_{17}H_{11}N_3$ requires C, 79·4; H, 4·3; N, 16·3%).

XUM

Quaternisation of 9-*Phenyl*-2 : 3 : 10-*triazaphenanthrene*.—(*a*) The base (1·2 g.), methyl iodide (4·8 c.c.), and methanol (24 c.c.) were heated under reflux for 3 hr. The solid was washed successively with methanol and ether and crystallised from water (*ca.* 140 c.c.), giving orange-yellow blades of a *monomethiodide* (1·5 g.), m. p. 285—287° (decomp.) (Found: C, 53·9; H, 3·4; N, 10·3; I, 32·4. $C_{18}H_{14}N_3I$ requires C, 54·1; H, 3·5; N, 10·5; I, 31·8%).

(*b*) The base (0·3 g.), dimethyl sulphate (0·3 c.c.), and nitrobenzene (30 c.c.) were heated at 160° (oil-bath) for 3 hr. The solution was diluted with ether, and the product extracted with water. The extract was saturated with potassium iodide, and the precipitate crystallised from water, forming orange-yellow microblades (270 mg.), m. p. 285—287° (decomp.), alone and on admixture with a sample prepared as above.

4-*Nitrobenzamido*-5-*phenylpyridazines*.—4-Amino-5-phenylpyridazine (2·5 g.) and *o*-nitrobenzoyl chloride (from 3·0 g. of the acid) in dry pyridine (20 c.c.) were heated on the steam-bath for 2½ hr. The product [from methanol (charcoal)] formed plates of 4-o-*nitrobenzamido*-5-*phenylpyridazine* (2·7 g., 58%), m. p. 216—218° (Found: C, 63·4; H, 3·4; N, 17·9. $C_{17}H_{12}O_3N_4$ requires C, 63·7; H, 3·8; N, 17·5%).

Prepared similarly, 4-m-*nitrobenzamido*-5-*phenylpyridazine* formed prisms (7·8 g., 83%; from 5·0 g.), m. p. 198—199°, from acetone (Found: C, 63·7; H, 3·9; N, 17·5%), and the 4-p-*nitrobenzamido*-compound, blades (5·9 g., 79%; from 4·0 g.), m. p. 216—217°, from methanol (Found: C, 63·5; H, 4·0; N, 18·0%).

9-p-*Nitrophenyl*-2 : 3 : 10-*triazaphenanthrene*.—Phosphorus pentoxide (*ca.* 18 g.) was added in three portions to a stirred solution of 5-*p*-nitrobenzamido-4-phenylpyridazine (6 g.) in dry nitrobenzene (180 c.c.) at *ca.* 140°, and the mixture was stirred at *ca.* 180° for 6 hr., with further addition of phosphorus pentoxide (*ca.* 9 g.) after 3 hr. Water was carefully added and the mixture was basified with 6N-sodium hydroxide, steam distilled, and filtered hot. The brown material was crystallised from nitromethane (charcoal), yielding fine needles of 9-p-*nitrophenyl*-2 : 3 : 10-*triazaphenanthrene* (3·9 g., 69%), m. p. 300—301° (Found: C, 67·3; H, 3·4; N, 18·9. $C_{17}H_{10}O_2N_4$ requires C, 67·5; H, 3·3; N, 18·6%).

9-p-*Aminophenyl*-2 : 3 : 10-*triazaphenanthrene*.—A warm solution of stannous chloride (10 g.) in concentrated hydrochloric acid (10 c.c.) and the nitro-compound (2 g.) were heated on the steam-bath for ½ hr. The mixture was then poured into 6N-sodium hydroxide, the solution heated almost to boiling, and the yellow precipitate crystallised from alcohol, furnishing golden-yellow needles of 9-p-*aminophenyl*-2 : 3 : 10-*triazaphenanthrene* (1·6 g., 89%), m. p. 305—307° (Found: C, 74·7; H, 4·3; N, 19·65. $C_{17}H_{12}N_4$ requires C, 75·0; H, 4·4; N, 20·6%).

Quaternisation of 9-p-*Aminophenyl*-2 : 3 : 10-*triazaphenanthrene*.—The base (2 g.) and methyl iodide (10 c.c.) in nitromethane (400 c.c.) were heated under reflux for 4 hr. The crude salt (2·12 g.), m. p. 320—323° (decomp.), was crystallised from a large volume of alcohol, yielding fine red needles of the *monomethiodide*, m. p. 323—324° (decomp.) (Found: C, 51·2; H, 3·8; N, 13·3; I, 31·2. $C_{18}H_{14}N_4I$ requires C, 52·05; H, 3·7; N, 13·5; I, 30·65%).

9-m-*Nitrophenyl*-2 : 3 : 10-*triazaphenanthrene*.—Prepared as described for the *p*-nitrophenyl compound 9-m-*nitrophenyl*-2 : 3 : 10-*triazaphenanthrene* crystallised from acetonitrile (charcoal) in fluffy needles (0·7 g., 74%; from 1 g.), m. p. 251—254° raised by a further crystallisation to 255—257° (Found: C, 67·5; H, 3·2; N, 17·8%).

9-m-*Aminophenyl*-2 : 3 : 10-*triazaphenanthrene*.—The nitro-compound (2·5 g.) was reduced as described for the *p*-isomer. Crystallisation from alcohol yielded yellow blades of 9-m-*aminophenyl*-2 : 3 : 10-*triazaphenanthrene* (1·8 g., 80%), m. p. 245—246° (Found: C, 74·15; H, 4·65; N, 21·0%).

5-p-*Methoxyphenylpyridazine*-4-*carboxylic Acid*.—The corresponding dicarboxylic acid [20 g., m. p. 148—150° (efferv.); prepared by oxidation of 4-*p*-methoxyphenylcinnoline] was heated with 2-ethoxyethanol (40 c.c.) under reflux until evolution of gas almost ceased (15 min.). The crude product was washed with a little alcohol. Crystallisation from alcohol (charcoal) gave needles of the *acid* (11 g., 62% based upon 4-*p*-methoxyphenylcinnoline), m. p. 206—208° (decomp.) (lit.,[18] m. p. 205°).

5-(4-*Methoxy*-3-*nitrophenyl*)*pyridazine*-4-*carboxylic Acid*.—A solution of 5-*p*-methoxyphenylpyridazine-4-carboxylic acid (37 g.) in dilute nitric acid (1000 c.c.) was evaporated almost to dryness on the steam-bath; the yellow solid was triturated with cold water (*ca.* 1 l.), filtered, and washed thoroughly with water. This crude material was dissolved in boiling dilute nitric acid and water added to give fine pale yellow needles of 5-(4-methoxy-3-nitrophenyl)pyridazine-4-carboxylic acid (31 g.), m. p. 232—234° (decomp.). Lit.,[18] m. p. 230° (decomp.).

The *methyl ester* (prepared by use of diazomethane in dioxan) formed yellow blades (78%), m. p. 151—153°, from alcohol (Found: C, 54·1; H, 4·0; N, 14·9. $C_{13}H_{11}O_5N_3$ requires C, 54·0; H, 3·8; N, 14·5%).

4-Carbamoyl-5-(4-methoxy-3-nitrophenyl)pyridazine.—A suspension of powdered methyl ester (30 g.) in methanol (1·5 l.) was saturated at 5° with ammonia and set aside at room temperature with occasional shaking for 14 days, being resaturated with ammonia after 7 days. The precipitate and material recovered from the filtrate by concentration and precipitation was crystallised from alcohol, yielding pale yellow blades of the *amide* (20·5 g., 72%), m. p. 233—234° (decomp.) (Found: C, 52·4; H, 3·8; N, 21·2. $C_{12}H_{10}O_4N_4$ requires C, 52·55; H, 3·7; N, 20·4%).

4-Amino-5-(4-methoxy-3-nitrophenyl)pyridazine.—Powdered 4-carbamoyl-5-(4-methoxy-3-nitrophenyl)pyridazine (10 g.) was added in one portion to aqueous potassium hypobromite [from bromine (2·0 c.c.) and potassium hydroxide (10 g.) in water (100 c.c.) at 0°] and the mixture stirred at 0° for 7 hr. The solution was heated on the steam-bath for 40 min. and the crude amine then crystallised from acetone, giving needles of *4-amino-5-(4-methoxy-3-nitrophenyl)pyridazine* (4·5 g., 50%), m. p. 199—201° (decomp.) (Found: C, 53·9; H, 4·4; N, 22·35. $C_{11}H_{10}O_3N_4$ requires C, 53·7; H, 4·1; N, 22·8%).

4-Benzamido-5-(4-methoxy-3-nitrophenyl)pyridazine.—The foregoing amine was benzoylated by benzoyl chloride–pyridine in boiling chlorobenzene for 32 hr. Golden needles (9·9 g.), m. p. 206—210°, separated from the cold solution, and recrystallisation from absolute ethanol (charcoal) gave the *benzamide* as pale yellow needles (62%), m. p. 220—221° (Found: C, 61·8; H, 3·8; N, 15·3. $C_{18}H_{14}O_4N_4$ requires C, 61·7; H, 4·0; N, 16·0%).

4-(3-Amino-4-methoxyphenyl)-5-benzamidopyridazine.—(*a*) The foregoing nitro-compound (0·6 g.) was heated in ethanol (60 c.c.) at *ca.* 90° with hydrogen under pressure (*ca.* 100 atm.) for 2½ hr., in the presence of 5% palladised charcoal. The solution was filtered and evaporated to dryness, and the residue crystallised (twice) from methanol (charcoal), yielding needles of the *amine* (0·27 g.), m. p. 185—186° (Found: C, 67·4; H, 5·2; N, 17·1. $C_{18}H_{16}O_2N_4$ requires C, 67·5; H, 5·0; N, 17·5%).

(*b*) The powdered nitro-compound (4 g.) was added portionwise to stannous chloride reagent [20] (150 c.c.) and set aside at room temperature. Next day, the white solid was treated with ice and an excess of dilute ammonia solution. A chloroform extract was washed, dried ($MgSO_4$), and evaporated (finally with the aid of benzene under reduced pressure). The residue crystallised from methanol (charcoal) as pale yellow needles (2·7 g., 74%), m. p. 185—186° alone and on admixture with a sample prepared as above.

4-(3-Acetamido-4-methoxyphenyl)-5-benzamidopyridazine.—The foregoing amine was acetylated with acetic anhydride on the steam bath for ½ hr.. *4-(3-Acetamido-4-methoxyphenyl)-5-benzamidopyridazine* (0·3 g., 66%) formed flat needles, m. p. 189—190°, from acetone (charcoal) (Found: C, 66·1; H, 4·9; N, 15·2. $C_{20}H_{18}O_3N_4$ requires C, 66·3; H, 5·0; N, 15·5%).

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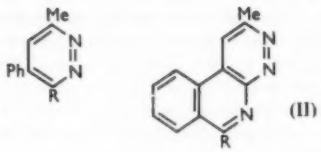
[20] Albert and Linnell, *J.*, 1936, 1617.

2. *Triazaphenanthrenes. Part IV.* Some 9-Aryl-3-methyl-1 : 2 : 10-triazaphenanthrenes.*

By C. M. Atkinson and R. E. Rodway.

9-Aryl-3-methyl-1 : 2 : 10-triazaphenanthrenes (II) have been prepared by cyclisation of arylamidopyridazines (I; R = NH·COAr). The derived monomethiodides were biologically inactive.

Previous papers have described the synthesis of triazaphenanthrenes from quinolines and cinnolines. Work based on pyridazine derivatives (I) is now described.



(I) (II)

The pyridazine (I; R = OH) was prepared by dehydrogenation of the pyridazinone obtained from hydrazine and α-phenyl-lævulic acid (cf. ref. 1); the latter being synthesised by a modification of Ruhemann's method [2] from 3-benzylidenepentane-2 : 4-dione [3] which also was prepared by an improved method.[4]

Methods applicable in the cinnoline [5] or quinoline [6] series did not convert the corresponding chloro-compound (I; R = Cl) into the amine (I; R = NH_2), but use of urea in a sealed tube gave reproducible yields. Treatment of the benzamido-compound (I; R = NH·COPh) with phosphorus oxychloride or phosphorus pentoxide in nitrobenzene at 180° did not give a useful product but some success was achieved with phosphorus pentoxide in boiling nitrobenzene. However, a melt of aluminium chloride and sodium chloride gave over 50% of the triazaphenanthrene (II; R = Ph). The *p*-nitrobenzamido-derivative (I; R = NH·CO·C_6H_4·NO_2) was, however, cyclised in low yields by phosphorus pentoxide in nitrobenzene, other variations being useless.

Quaternisation of 3-methyl-9-phenyl-1 : 2 : 10-triazaphenanthrene with methanolic methyl iodide yielded a mixture of two monomethiodides, but only one monomethiodide could be obtained from the 9-*p*-nitrophenyl analogue. These salts were inactive against the organisms listed in the preceding paper.

Experimental

3-Benzylidenepentane-2 : 4-dione.—A homogeneous mixture of benzaldehyde (4·0 moles, 404 c.c.), acetylacetone (4·0 moles, 424 c.c.), and piperidine (3·2 c.c.) was set aside at room temperature and shaken occasionally. After 6 days the mixture was diluted with ether (750 c.c.), and piperidine removed by washing with dilute hydrochloric acid followed by water. The ethereal layer was dried ($MgSO_4$), the solvent removed, and the residue distilled, yielding unchanged materials followed by 3-benzylidenepentanedione (470 g., 63%; b. p. 149—150°/*ca.* 4 mm.). The semicarbazone separated from alcohol in glistening plates, m. p. 223—224° (decomp.) (Found: C, 63·5; H, 6·1; N, 17·6. Calc. for $C_{13}H_{15}O_2N_3$: C, 63·7; H, 6·2; N, 17·1%). The literature [7] m. p. is 210° (decomp.).

* Part III, preceding paper.

[1] Overend and Wiggins, *J.*, 1947, 239.
[2] Ruhemann, *J.*, 1904, **85**, 1451.
[3] Knoevenagel and Faber, *Ber.*, 1898, **31**, 2773; Knoevenagel and Werner, *Annalen*, 1894, **281**, 79.
[4] Courts and Petrow, *J.*, 1952, 1; Ruhemann, *J.*, 1903, 1373; Kuhn, *J.*, 1938, 605; Baker and Lapworth, *J.*, 1925, 560.
[5] Keneford, Schofield, and Simpson, *J.*, 1948, 358.
[6] Backeberg and Marais, *J.*, 1942, 381.
[7] Ruhemann and Watson, *J.*, 1904, **85**, 460.

3-α-*Cyanobenzylpentane*-2 : 4-*dione*.—Potassium cyanide (144 g., AnalaR) in water (288 c.c.) was added during 1½ hr. at <3° to a stirred solution of 3-benzylidenepentane-2 : 4-dione (230 g.) in alcohol (2 l.). The solution was then stirred for a further hour at 0° and acidified at <10° by slow addition of dilute hydrochloric acid (1½ l.). The precipitate was washed with a small amount of cold water; after prolonged drying in a vacuum desiccator (H_2SO_4) the crude product (198 g., 75%) had m. p. 118—121°. Two crystallisations from aqueous alcohol provided needles of the cyano-compound, m. p. 127—129° (Ruhemann [2] gave m. p. 127—128°), which decomposed slowly at room temperature.

β-*Acetyl*-α-*phenylpropionic Acid*.—Crude 3-α-cyanobenzylpentane-2 : 4-dione (308 g.) and potassium hydroxide (500 g.) in water (2·5 l.) were heated under reflux for *ca.* 100 hr. The acid was isolated by acidification with dilute hydrochloric acid and extraction with ether. Evaporation of the extract and crystallisation of the residue from water (*ca.* 6 l.) (charcoal) gave pure β-acetyl-α-phenylpropionic acid as irregular plates (156 g.), m. p. 127—129° (Ruhemann [2] gave m. p. 126°). More (12 g.) pure acid was recovered from the mother liquors (total yield 168 g., 61%) (Found: C, 68·7; H, 6·5. Calc. for $C_{11}H_{12}O_3$: C, 68·7; H, 6·3%).

6-*Methyl*-4-*phenylpyridazin*-3-*one*.—A suspension of acetylphenylpropionic acid (150 g.) in alcohol (300 c.c.) was heated under reflux with hydrazine hydrate (45 c.c.; 99—100%) for 4 hr. The warm solution was stirred into water (2½ l.); the precipitate was washed with water, dried in a vacuum desiccator (H_2SO_4), and crystallised (charcoal) from benzene–light petroleum (b. p. 60—80°), giving needles of 6-*methyl*-4-*phenylpyridazin*-3-*one* (125 g., 85%), m. p. 121—123° (Found: C, 70·4; H, 6·7; N, 15·45. $C_{11}H_{12}ON_2$ requires C, 70·2; H, 6·4; N, 14·9%).

Hydrobromide. Bromine (24 c.c.) was added slowly to the pyridazinone (60 g.) in acetic acid (240 c.c.) without external cooling. The solid was collected next day, washed with acetic acid until colourless and then with ether, and crystallised from acetic acid, yielding the hydrobromide as brittle needles, m. p. 251—254° (decomp.) (crude yield 89%).

3-*Hydroxy*-6-*methyl*-4-*phenylpyridazine*.—(*a*) The hydrobromide (2·2 g.) was hydrolysed during crystallisation from aqueous alcohol and yielded glistening needles of the *base*, m. p. 172—174° (Found: C, 70·5; H, 5·6; N, 15·15. $C_{11}H_{10}ON_2$ requires C, 70·95; H, 5·4; N, 15·05%). (*b*) The crude hydrobromide [153 g., m. p. 250—253° (decomp.)] was treated with an excess of dilute ammonia solution and then extracted with chloroform, and the extract washed and dried ($MgSO_4$). The material (102 g., 96%), m. p. 166—168°, obtained by evaporation of the solvent, was suitable for direct conversion into the 3-chloro-compound.

3-*Chloro*-6-*methyl*-4-*phenylpyridazine*.—3-Hydroxy-6-methyl-4-phenylpyridazine (100 g.) was heated with phosphorus oxychloride (400 c.c.) on the steam-bath for 1½ hr., after which the excess of phosphorus oxychloride was removed under reduced pressure, finally with the aid of benzene. The residue was treated with crushed ice, made alkaline with 6N-sodium hydroxide, and extracted with methylene chloride. The combined extracts were washed free from alkali, dried ($MgSO_4$), and evaporated. The solid was crystallised twice (charcoal) from light petroleum (b. p. 90—110°) giving silky needles of 3-*chloro*-6-*methyl*-4-*phenylpyridazine*, m. p. 110—112° (Found: C, 64·7; H, 4·8; N, 13·6; Cl, 17·7. $C_{11}H_9N_2Cl$ requires C, 64·5; H, 4·4; N, 13·7; Cl, 17·3%).

6-*Methyl*-3-*phenoxy*-4-*phenylpyridazine*.—A stream of dry ammonia was passed into the 3-chloro-compound (2 g.) dissolved in phenol (10 g.) at 180° (oil-bath) for 40 min. The mixture was then cooled, diluted with ether, washed with dilute sodium hydroxide followed by water, and then dried ($MgSO_4$). Evaporation gave a pale yellow oil (2 g.) which crystallised; two crystallisations from light petroleum (b. p. 60—80°) (charcoal) gave glistening plates of 6-*methyl*-3-*phenoxy*-4-*phenylpyridazine* (1·85 g., 72%), m. p. 96—98° (Found: C, 77·7; H, 5·5; N, 10·85. $C_{17}H_{14}ON_2$ requires C, 77·8; H, 5·4; N, 10·7%).

3-*Amino*-6-*methyl*-4-*phenylpyridazine*.—Powdered 3-chloro-6-methyl-4-phenylpyridazine (8 g.) and urea (40 g.) were heated in a sealed tube for 40 hr. at 190°. The product was digested with boiling dilute sodium hydroxide (100 c.c.), cooled, filtered off, and washed with water. The 3-*amino*-6-*methyl*-4-*phenylpyridazine*, m. p. 191—193° formed small glistening needles (77%; from benzene) (Found: C, 71·6; H, 6·1; N, 21·5. $C_{11}H_{11}N_3$ requires C, 71·3; H, 6·0; N, 22·7%).

3-*Benzamido*-6-*methyl*-4-*phenylpyridazine*.—The amine was benzoylated with benzoyl chloride and pyridine under reflux for 6 hr. 3-*Benzamido*-6-*methyl*-4-*phenylpyridazine* (71%) formed clusters of prisms, m. p. 208—210°, from alcohol (Found: C, 75·2; H, 5·3; N, 15·0. $C_{18}H_{15}ON_3$ requires C, 74·7; H, 5·2; N, 14·5%).

XUM

3-*Methyl*-9-*phenyl*-1 : 2 : 10-*triazaphenanthrene*.—(*a*) 3-Benzamido-6-methyl-4-phenylpyridazine (8 g.) and a powdered mixture of aluminium chloride (29·6 g.) and sodium chloride (10·4 g.) were heated and stirred in an oil-bath (*ca.* 220°) for 4½ hr. Crushed ice (*ca.* 300 g.) was added to the cold mixture which was then heated, cooled, and filtered (filtrate A). The residue was digested with warm dilute sodium hydroxide, filtered off, washed, dried, and crystallised twice from methanol (charcoal), giving pale yellow needles (4·0 g., 54%), m. p. 254—256°, of 3-*methyl*-9-*phenyl*-1 : 2 : 10-*triazaphenanthrene* (Found: C, 79·8; H, 5·0; N, 14·8. $C_{19}H_{13}N_3$ requires C, 79·7; H, 4·9; N, 15·5%).

Filtrate A was made alkaline with 6N-sodium hydroxide, and the dried precipitate (1·4 g.) digested with boiling chloroform. The digest, on evaporation to dryness and crystallisation (twice) from methanol, yielded rosettes of broad blades, m. p. 191—193° alone and on admixture with authentic 3-amino-6-methyl-4-phenylpyridazine.

(*b*) To a solution of the 3-benzamide (0·4 g.) in dry nitrobenzene (12 c.c.) at 140° phosphorus pentoxide (1·5 g.) was added and the mixture heated under reflux in an oil-bath for 3½ hr. Water was carefully added and nitrobenzene then removed by steam-distillation. The residual aqueous portion was filtered hot and the filtrate made alkaline with dilute sodium hydroxide. The solid (150 mg.; m. p. 226—246°) was dissolved in acid and reprecipitated with alkali. Extraction of the dry product with chloroform yielded material which crystallised from methylene chloride as straw-coloured needles, m. p. 254—256° alone and when mixed with a sample prepared as above.

Quaternisation of 3-*Methyl*-9-*phenyl*-1 : 2 : 10-*triazaphenanthrene*.—(*a*) The base (2 g.) was heated under reflux with methyl iodide (5 c.c.) in nitromethane (30 c.c.) for 45 min., and the orange needles (0·6 g.) which separated on cooling crystallised twice from nitromethane, giving pure α-*monomethiodide*, m. p. 243—246° (decomp.) (Found: C, 54·75; H, 4·6; N, 9·75; I, 30·6. $C_{19}H_{16}N_3I$ requires C, 55·2; H, 3·9; N, 10·2; I, 30·7%).

The initial filtrate was treated with an excess of dry ether, and the precipitate (2·6 g.) crystallised twice from alcohol, giving dark red blades of pure β-*monomethiodide*, m. p. 212—213° (decomp.) (Found: C, 54·9; H, 4·6; N, 10·0; I, 30·3%).

(*b*) The base (0·3 g.) was heated with dimethyl sulphate (0·6 c.c.) in nitrobenzene (30 c.c.) at 150—160° (oil-bath) for 4 hr. The mixture was cooled, diluted with ether, and extracted with water. The aqueous extract was saturated with potassium iodide and the precipitate crystallised from alcohol, providing tawny needles (0·04 g.), m. p. 158—160° (decomp.); recrystallisation gave a mixture of blades and fine needles. Concentration of the mother-liquor furnished dark red blades (0·19 g.), m. p. 212—213° (decomp.) not depressed on admixture with the β-monomethiodide obtained as above.

3-m-*Nitrobenzamido*-6-*methyl*-4-*phenylpyridazine*.—3-Amino-6-methyl-4-phenylpyridazine (2 g.), *m*-nitrobenzoyl chloride (from 2·4 g. of the corresponding acid), and pyridine (20 c.c.) were heated on the steam-bath for 4 hr. 6-*Methyl*-3-m-*nitrobenzamido*-4-*phenylpyridazine* formed feathery needles (from acetone) (3·0 g., 83%), m. p. 216—218° (Found: C, 64·6; H, 4·55; N, 15·25. $C_{18}H_{14}O_3N_4$ requires C, 64·7; H, 4·2; N, 16·8%).

6-*Methyl*-3-p-*nitrobenzamido*-4-*phenylpyridazine*.—Similarly prepared the p-*nitrobenzamide* formed pale yellow crystals (72%), m. p. 227—229° (from methanol) (Found: C, 64·5; H, 4·0; N, 15·2%).

3-*Methyl*-9-p-*nitrophenyl*-1 : 2 : 10-*triazaphenanthrene*.—6-*Methyl*-3-p-*nitrobenzamido*-4-*phenylpyridazine* (6 g.) in dry nitrobenzene (180 c.c.) and phosphorus pentoxide (*ca.* 12 g.) were stirred at *ca.* 180° for 7 hr., more phosphorus pentoxide (6 g.) being added after 3½ hr. 3-*Methyl*-9-p-*nitrophenyl*-1 : 2 : 10-*triazaphenanthrene* formed pale yellow blades (0·86 g., 15%), m. p. 338—339° (decomp.), from nitromethane (Found: C, 67·5; H, 3·9; N, 17·4. $C_{18}H_{12}O_2N_4$ requires C, 68·35; H, 3·8; N, 17·7%).

Quaternisation of 3-*Methyl*-9-p-*nitrophenyl*-1 : 2 : 10-*triazaphenanthrene*.—The base (1 g.), methyl iodide (20 c.c.), and nitromethane (200 c.c.) were heated under reflux for 1 hr. The solution was then concentrated to *ca.* 50 c.c., cooled, and diluted with ether. The precipitate after three crystallisations from methanol gave dark red blades of a *monomethiodide*, m. p. 218—220° (decomp.) (Found: C, 48·8; H, 3·5; N, 11·9; I, 27·6. $C_{19}H_{15}O_2N_4I,\frac{1}{2}H_2O$ requires C, 48·8; H, 3·5; N, 12·1; I, 27·2%).

Nitration of 3-*Chloro*-6-*methyl*-4-*phenylpyridazine*.—Powdered 3-chloro-6-methyl-4-phenylpyridazine (48 g.) was added portionwise to stirred fuming nitric acid (160 c.c.), below 10°, and the resultant solution kept at room temperature; after 3 days the mixture was poured on ice

and water (*ca.* 1 l.) and basified with dilute ammonia solution. The product gave by three recrystallisations from methanol (charcoal) needles of a *mononitro-derivative* of 3-chloro-6-methyl-4-phenylpyridazine (32·7 g., 56%), m. p. 221—223° (Found: C, 53·3; H, 3·5; N, 16·3; Cl, 14·2. $C_{11}H_8O_2N_3Cl$ requires C, 52·8; H, 3·2; N, 16·8; Cl, 14·2%).

3-*Amino*-6-*methyl*-4-x-*nitrophenylpyridazine*.—Powdered 3-chloro-compound (8 g.) and urea (40 g.) were heated in a sealed tube at 190° for *ca.* 30 hr. The product was digested with hot dilute sodium hydroxide and then filtered cold, the solid taken up in dilute acetic acid, the solution filtered (charcoal), and solid reprecipitated with alkali. Extraction with boiling chloroform, evaporation of the filtered extract, and crystallisation of the residue from acetone (charcoal) gave yellow rectangular prisms of 3-*amino*-6-*methyl*-4-x-*nitrophenylpyridazine* (3·5 g., 48%), m. p. 221—223° (Found: C, 57·2; H, 4·5; N, 24·5. $C_{11}H_{10}O_2N_4$ requires C, 57·4; H, 4·4; N, 24·3%).

3-*Benzamido*-6-*methyl*-4-x-*nitrophenylpyridazine*.—Prepared in the usual way from the foregoing amine 3-*benzamido*-6-*methyl*-4-x-*nitrophenylpyridazine* (4·0 g., 69%) formed blades (from ethanol), m. p. 198—200° (Found: C, 64·1; H, 4·2; N, 16·65. $C_{18}H_{14}O_3N_4$ requires C, 64·7; H, 4·2; N, 16·8%).

4-x-*Aminophenyl*-3-*benzamido*-6-*methylpyridazine*.—Powdered 3-benzamido-6-methyl-4-*x*-nitrophenylpyridazine (4 g.) was added to stannous chloride reagent [8] (120 c.c.). After 3½ hr. at room temperature with occasional shaking the mixture was filtered and the white granular precipitate treated with ice and an excess of dilute ammonia. The resultant mixture was extracted five times with chloroform and the washed and dried ($MgSO_4$) extract was evaporated to yield 4-x-*aminophenyl*-3-*benzamido*-6-*methylpyridazine* (2·8 g., 77%), yellow prisms (2·5 g., 69%), m. p. 205—207° (from alcohol) (Found: C, 70·7; H, 5·2; N, 18·0. $C_{18}H_{16}ON_4$ requires C, 71·0; H, 5·3; N, 18·4%).

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[8] Albert and Linnell, *J.*, 1936, 1617.

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3. *The Chemical Effects of γ-Radiation on Organic Systems. Part III.*[1] *The Action of Radiation on Triethylamine Alone or Mixed with Bromobenzene.*

By G. A. SWAN, P. S. TIMMONS, and D. WRIGHT.

Two new bases, *meso*- and racemic 2 : 3-bisdiethylaminobutane (II), have been isolated from triethylamine which had been irradiated with γ-rays and have also been synthesised chemically. When the irradiation was carried out in the presence of bromobenzene, in addition to these two bases, diethylaniline, diphenyl, and triethylamine hydrobromide were obtained.

PREVIOUS work [1] has shown that the action of γ-radiation on alcohols $R{\cdot}CH_2{\cdot}OH$ results in the formation of radicals $R{\cdot}CH(OH){\cdot}$, *i.e.*, the hydroxyl group facilitates homolysis of the C–H bond in the system H–C(–)–O–. Following the well-known analogy between bivalent oxygen and tervalent nitrogen in organic compounds it has now been shown that a similar effect occurs in the system H–C(–)–N(–)–. Thus irradiation of triethylamine with γ-rays led to *meso*- and racemic-2 : 3-bisdiethylaminobutane (II), presumably formed through the radical (I):

$$CH_3{\cdot}CH_2{\cdot}NEt_2 \rightsquigarrow CH_3{\cdot}\dot{C}H{\cdot}NEt_2 \longrightarrow Et_2N{\cdot}CH(CH_3){-}CH(CH_3){\cdot}NEt_2$$
(I) (II)

[1] Part II, Swan and Wright, *J.*, 1958, 4673.

The *meso*- and the racemic form of this base were formed in approximately equal amounts (*G* value for the crude mixture 2·9) and were separated by partition chromatography with a phosphate buffer of pH 6·5 on kieselguhr as the stationary phase and ether as the mobile phase, in a manner experimentally similar to that used by Evans and Partridge [2] for the separation of a mixture of hyoscyamine and scopolamine. The *meso*-base passed rapidly through the column with the ether, the racemic base remaining on the column, from which it was later isolated by treatment with sodium hydroxide solution and ether. This difference could scarcely be due to the difference in basic strength between the two isomers and (in any case) the racemic appeared to be weaker than the *meso*-base. It is probably due to the fact that in the most stable conformation of the *meso*-form similar groups achieve maximum separation, so that the two basic groups are too far apart to form a chelate phosphate, while in the racemic form chelation can occur. This was confirmed by the fact that no separation occurs when the phosphate buffer is replaced by an acetate buffer of the same pH.

Neither form of 2 : 3-bisdiethylaminobutane appears to have been described previously, so we synthesised the two isomers by alkylation of 2 : 3-diaminobutane, obtained by reduction of dimethylglyoxime. We have here a synthesis of two new compounds by irradiation, a method which moreover involves less work than the chemical synthesis. It is possible that other tertiary amines $(R{\cdot}CH_2)_3N$ behave similarly. Indeed, from benzylamine we have obtained *meso*-stilbenediamine; we hope to report more fully on this aspect later.

We also irradiated a 1 : 10—25 molar mixture of triethylamine and bromobenzene. Triethylamine hydrobromide crystallised [*G*(HBr 6—6·4], and it was shown by a tracer experiment that more than 90% of the hydrogen of this hydrogen bromide arose from the triethylamine and not from the bromobenzene. From the non-basic portion of the residual irradiation mixture diphenyl was isolated with $G = 0{\cdot}65$, but probably much loss was involved.

The ultraviolet spectrum of the basic product of b. p. 100—130° (bath-temp.)/1 mm. resembled that of diethylaniline, although the extinction coefficient was much lower (3800 instead of 15,000 at 2600 Å). Chromatography of this fraction in a phosphate buffer of pH 6·5 afforded pure *meso*-2 : 3-bisdiethylaminobutane, and in a similar buffer of pH 5 afforded impure aniline ($G < 0{\cdot}1$), racemic 2 : 3-bisdiethylaminobutane, and a compound of acetophenone-like odour, which failed to give a 2 : 4-dinitrophenylhydrazone. A basic fraction of b. p. > 130°/12 mm. was not identified: we failed to isolate diethyl-1-phenylethylamine from it, though we synthesised this compound for a study of its chromatographic behaviour. We also irradiated a mixture of benzyl alcohol and triethylamine, but were unable to establish the formation of any coupling products of a radical $Et_2N{\cdot}CHMe{\cdot}$ with $Ph{\cdot}CH_2{\cdot}$ or $Ph{\cdot}CH(OH){\cdot}$: the basic product was mainly 2 : 3-bisdiethylaminobutane and the small amount of higher-boiling material failed to yield crystalline derivatives.

The formation of diethylaniline from triethylamine and bromobenzene involves fission of a C–N bond, but it is not clear whether this is due to direct radiolysis:

$$Et_3N{\cdot}Et \longrightarrow Et_3N{\cdot} + {\cdot}Et$$

or is the result of a secondary reaction (*e.g.*, oxidation) of the primarily formed radical $Et_2N{\cdot}CHMe{\cdot}$. However, a large peak at mass number 72 points to the ready fission of the C–N bond of triethylamine in the mass-spectrometer. Bamford [3] reported that photolysis of trimethylamine gave hydrogen, methane, ethane, and polymers, and Gesser, Mullhaupt and Griffiths [4] reported the formation of an unidentified "liquid" instead of polymer. The production of ethane suggests the formation of $Me_2N{\cdot}$ and $Me{\cdot}$ radicals, and the former might give rise to tetramethylhydrazine: Rice and Grelecki's [5] isolation

[2] Evans and Partridge, *Quart. J. Pharm. Pharmacol.*, 1948, **12**, 399.
[3] Bamford, *J.*, 1939, 17.
[4] Gesser, Mullhaupt, and Griffiths, *J. Amer. Chem. Soc.*, 1957, **79**, 4834.
[5] Rice and Grelecki, *ibid.*, p. 2679.

of the $Me_2N\cdot$ radical as a violet solid, stable at −196°, but giving tetramethylhydrazine at −160° is relevant. The latter authors [6] also suggested the formation of the $Me\cdot NH\cdot CH_2\cdot$ radical from dimethylamine in the field of a high-frequency oscillator, where there was no evidence of the formation of tetramethylhydrazine. Thermal decomposition of trimethylamine yields mainly methane and methylmethyleneimine together with small amounts of hydrogen and ethane.[7]

Cosgrove and Waters [8] obtained acetaldehyde, glyoxal, and diethylamine by the action of *N*-bromosuccinimide on triethylamine, and Braude and Waight [9] isolated triethylamine hydrobromide and succinimide from the same reaction. We have repeated the reaction to ascertain whether 2 : 3-bisdiethylaminobutane was also formed; but we were unable to isolate it. More recent work by Dunstan and Henbest [10] has, however, indicated that the reaction with *N*-bromosuccinimide takes the course:

$$2Et_3N + Br\cdot N(CO\cdot CH_2)_2 \longrightarrow Et_2N\cdot CH{:}CH_2\cdot + Et_3N{,}HBr + NH(CO\cdot CH_2)_2$$

$$Et_2N\cdot CH{:}CH_2 + H_2O \longrightarrow Et_2NH + CH_3\cdot CHO$$

Buckley, Dunstan, and Henbest have also shown that triethylamine is dehydrogenated to diethylvinylamine by chloranil [11] or benzoyl peroxide,[12] the former case being consistent with hydride-ion transfer from the amine to the quinone, yielding $Et_2N\cdot CHMe^+$, followed by loss of proton, although single-electron transfer could not be excluded. Our observation that the radical $Et_2N\cdot CHMe\cdot$ appears to dimerise readily supports the hydride-ion transfer mechanism in the chemically induced case. On the other hand, Buckley *et al.*[11] found that, although 1-ethylpiperidine undergoes a similar reaction with chloranil, reaction of the *N*-methyl compound proceeds only in the presence of light, indicating that attack on the piperidine ring is more difficult than on the ethyl group and perhaps pointing to a homolytic mechanism.

A chemical reaction which resembles, at least superficially, the radiation-induced reaction of triethylamine described above is that between amines and olefins, induced by peroxide or, in low yield, by light [13] [*e.g.*, the formation of (±)-coniine by the interaction of piperidine and propene in the presence of *tert.*-butyl peroxide]. The photo-sensitised oxidation of amines recently studied by Schenk [14] is a further example of free-radical attack on the H–C–N– group.

Experimental

Arrangements for the irradiations and spectroscopic measurements were as described in Part I.

meso- *and Racemic* 2 : 3-*Bisdiethylaminobutane* (II).—2 : 3-Diaminobutane (7 g.), prepared by reduction of dimethylglyoxime,[15] was converted into the dihydrochloride, which was boiled with methanol (90 ml.) for a few minutes. The insoluble *meso*-dihydrochloride (5·5 g.) was collected and when crystallised from aqueous methanol had m. p. >290°. Concentration of the methanol mother-liquors afforded the crude racemic dihydrochloride, m. p. 255°.

A mixture of *meso*-2 : 3-diaminobutane dihydrochloride (2·3 g.), ethyl iodide (8·9 g., 4 mol.), sodium carbonate (9 g.), and water (70 ml.) was refluxed for 20 hr. The basic material was extracted with ether and then warmed for 2 hr. with acetic anhydride (6 ml.) in benzene (6 ml.). The excess of anhydride was decomposed by washing with sodium carbonate solution, and the benzene layer was dried and distilled, giving *meso*-2 : 3-bisdiethylaminobutane (0·77 g.), b. p.

[6] Rice and Grelecki, *J. Phys. Chem.*, 1957, **61**, 824.
[7] Carter, Bosanquet, Silcocks, Travers, and Wilshire, *J.*, 1939, 495.
[8] Cosgrove and Waters, *J.*, 1949, 907.
[9] Braude and Waight, *J.*, 1952, 1116.
[10] Dunstan and Henbest, *J.*, 1957, 4905.
[11] Buckley, Dunstan, and Henbest, *J.*, 1957, 4880.
[12] *Idem, ibid.*, p. 4901.
[13] Urry, Juveland, and Stacey, *J. Amer. Chem. Soc.*, 1952, **74**, 6155.
[14] Schenk, *Angew. Chem.*, 1957, **69**, 579.
[15] Dickey, Fickett and Lucas, *J. Amer. Chem. Soc.*, 1952, **74**, 944; Strack and Schwaneberg, *Ber.*, 1934, **67**, 1006.

XUM

110° (bath-temp.)/15 mm., affording a *dihydrochloride*, m. p. 238° (from ethanol) (Found: C, 53·3; H, 11·45. $C_{12}H_{30}N_2Cl_2$ requires C, 52·8; H, 11·0%), and a *dipicrate*, m. p. 178° (Found: C, 44·05; H, 5·25. $C_{24}H_{34}O_{14}N_8$ requires C, 43·75; H, 5·15%).

The crude racemic dihydrochloride, when ethylated as above, gave a base, b. p. 100° (bath-temp.)/12 mm., yielding a picrate which was not homogeneous. A solution of this base (136 mg.) in ether was therefore passed through a column of kieselguhr (30 g.) and 0·5M-phosphate buffer of pH 6·5 (30 g.). The first 150 ml. of ether eluted 30 mg. of base which was discarded. The column was then treated with 20% sodium hydroxide solution; an ether extract of the eluate yielded racemic 2 : 3-bisdiethylaminobutane, affording a deliquescent *dihydrochloride*, m. p. 233° (Found: C, 52·7; H, 11·5%), and a *dipicrate*, m. p. 137° (from ethanol in which it is more soluble than is the *meso*-dipicrate) (Found: C, 43·7; H, 5·35%). As measured by the use of a glass electrode, a solution of the racemic dihydrochloride (14·8 mg.) in triply distilled water (10 ml.) had pH 2·9, whereas one of the *meso*-dihydrochloride (16·2 mg.) in water (10 ml.) had pH 4·1.

Irradiation of Triethylamine.—Pure triethylamine (275 ml.) was irradiated for 300 hr. (total dose $2·08 \times 10^{23}$ ev) and unchanged material was then removed by distillation. The residue (2 g.) distilled at 90—125°/30 mm. and consisted mainly of *meso*- and racemic 2 : 3-bisdiethylaminobutane. Part of this mixture (407 mg.) was separated into its components by partition chromatography, as described above. The first 100 ml. of ether yielded the *meso*-diamine (130·5 mg.), which with picric acid gave a 92% yield of pure picrate, m. p. and mixed m. p. 179°. Treatment of the column with sodium hydroxide solution then liberated crude racemic diamine (152·4 mg.) which was isolated by ether. This was purified by partition chromatography at pH 8, the later fractions yielding the pure racemic picrate, m. p. and mixed m. p. 136°. The picrate from the earlier fractions, after recrystallisation from ethanol, yielded the same, pure picrate. Chromatography at pH 7·0 or 7·4 failed to affect sharp separation from the impurity.

Irradiation of a Mixture of Triethylamine and Bromobenzene.—(*a*) A mixture of triethylamine (25 ml.) and bromobenzene (250 ml.) was irradiated for 144 hr. (total dose $2·37 \times 10^{23}$ ev). The precipitated triethylamine hydrobromide (4·3 g.) was collected and unchanged triethylamine was removed by distillation. The residue was extracted with 5N-hydrochloric acid. Basification of the extract followed by re-extraction with ether gave an oil (0·375 g.), b. p. 100—110° (bath-temp.)/15 mm., and a residue not distilling at 130°/10 mm. The bromobenzene was removed by distillation from the acid-washed irradiation product, and the residue was chromatographed on alumina, giving diphenyl, m. p. 69° (0·39 g.). (*b*) A similar experiment in which the same volume (275 ml.) of a 1 : 10 mol. mixture of triethylamine and bromobenzene was irradiated for 300 hr. (total dose $4·04 \times 10^{23}$ ev) yielded triethylamine hydrobromide (7·8 g.) and basic fractions: (i) b. p. 100—130° (bath-temp.)/12 mm. (0·52 g.), and (ii) residue, a black tar (2·35 g.). Fraction (i) was subjected to partition chromatography, with a phosphate buffer of pH 6·5. The first three ether fractions contained 137, 86, and 32 mg., respectively, of base. The third of these portions yielded a hydrochloride, m. p. 238°, and a highly insoluble picrate, m. p. 178°, identical with *meso*-2 : 3-bisdiethylaminobutane picrate (Found: C, 44·05; H, 5·25%). These three fractions were recombined and subjected to partition chromatography in a phosphate buffer of pH 5. The ether which passed through yielded a base (150 mg.) which gave diethylaniline picrate, m. p. and mixed m. p. 137—138° (Found: C, 50·55; H, 4·5. Calc. for $C_{16}H_{18}O_7N_4$: C, 50·8; H, 4·75%); this base, however, on distillation yielded two fractions, b. p. 75° (bath-temp.)/12 mm. and (the greater part), b. p. 115° (bath-temp.)/12 mm., the extraction coefficient of which (10,900 at 2600 Å) indicated the presence of 70% of diethylaniline, *meso*-2 : 3-Bisdiethylaminobutane was isolated from the pH 5 column by treatment with sodium hydroxide solution and ether. The impure racemic isomer was similarly isolated from the pH 6·5 column and was purified by partition chromatography in a phosphate buffer of pH 8, the first few ether fractions giving gummy picrates, but the later fractions yielding a picrate, m. p. 137°, identical with racemic 2 : 3-bisdiethylaminobutane picrate.

Fraction (ii) was subjected to partition chromatography at pH 6·5. Approximately 1 g. passed through with ether, but only a small proportion of this distilled at 160°/1 mm. (Found: C, 70·85, 71·75; H, 9·25, 9·1%) and this showed no characteristic ultraviolet absorption, only a gradual rise in optical density from 2900 to 2200 Å. No further base was eluted by ether or chloroform, but treatment of the column with 20% sodium hydroxide solution released 0·7 g. of unidentified base.

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Irradiation of a Mixture of Triethylamine and Bromodeuterobenzene.—Deuterobenzene [14] was brominated as described for the preparation of bromobenzene by Gattermann.[17] This bromodeuterobenzene (7·85 g.), the hydrogen of which contained 12·0% of deuterium, and triethylamine (5·05 g.) were irradiated for 70 hr. (total dose $3·61 \times 10^{21}$ ev), and the resulting triethylamine hydrobromide (92·6 mg.; m. p. 242—243°) was collected. The hydrogen of the salt was enriched with respect to deuterium to the extent of 0·068%. The deuterium content of these compounds was determined by Mr. P. Kelly, M.Sc. by combustion [18] and reduction of the resulting water by Graff and Rittenberg's procedure,[19] before mass-spectrometic assay. The result quoted in the introductory part of the paper was calculated by neglecting any isotope effect and is therefore bound to be inaccurate as it is known that hydrogen atoms are abstracted more easily than deuterium atoms.[20]

Diethyl-1-phenylethylamine.—A mixture of 1-phenylethylamine (12·1 g.), ethyl iodide (31·2 g., 2 mol.), sodium carbonate (21·2 g.), and water (200 ml.) was refluxed for 20 hr., cooled, and extracted with ether. The ether was removed from the dried extract, and the residue was warmed with acetic anhydride (10 ml.) and benzene (10 ml.) for 2 hr., cooled, treated with water and sodium carbonate solution, and extracted with ether. Distillation of the dried extract yielded the base (5·5 g.), b. p. 94°/12 mm., affording a *picrate*, m. p. 131°, from ethanol (Found: C, 52·95; H, 5·5. $C_{18}H_{22}O_7N_4$ requires C, 53·2; H, 5·4%).

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DEPARTMENT OF CHEMISTRY, KING'S COLLEGE (UNIVERSITY OF DURHAM), NEWCASTLE UPON TYNE, 1. [*Received, May 27th*, 1958.]

[14] Ingold, Raisin, and Wilson, *J.*, 1936, 1637.
[17] Gattermann, revised by Wieland, "Laboratory Methods of Organic Chemistry," Macmillan, London, 1937, p. 103.
[18] Anderson, Delabarre, and Bothner-By, *Analyt. Chem.*, 1952, **24**, 1298.
[19] Graff and Rittenberg, *ibid.*, p. 878.
[20] Burr, *J. Phys. Chem.*, 1957, **61**, 1477.

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4. *Polyfluoroarenes. Part I. Pentafluorophenol.*

By J. M. BIRCHALL and R. N. HASZELDINE.

Hexafluorobenzene, readily prepared by pyrolysis of tribromofluoromethane, has been converted into pentafluorophenol under mild conditions and in good yield; derivatives and properties of pentafluorophenol are described. Infrared spectroscopy reveals a characteristic ring vibration near 1520 cm.$^{-1}$ for pentafluorophenyl derivatives and suggests that appreciable aromatic character is associated with the ring. The decreased basicity of oxygen in pentafluorophenol causes less intermolecular hydrogen bonding than with phenol, and is reflected in its relatively low b. p. (143°); the possibility of intramolecular hydrogen bonding to the *ortho* fluorine atoms is considered.

ALTHOUGH many per- and poly-fluoroalkyl compounds are now known, very few compounds of type Ar_FX, where Ar_F is a perfluoroaryl group and X is a functional group, have been synthesised. Hexafluorobenzene was prepared by McBee *et al.*[1] but the route followed is unsatisfactory for synthesis on a larger scale. Earlier work by Désirant, only recently published,[2] provides the best method for the synthesis of hexafluorobenzene:

$$CFBr_3 \xrightarrow[\text{Pt tube}]{630\text{-}640^\circ} C_6F_6$$

Hexafluorobenzene has since been obtained [3] by dehydrofluorination of a nonafluoro*cyclo*hexane, but the preparation of suitable pure precursors of this type is tedious.

[1] McBee, Lindgren, and Ligett, *Ind. Eng. Chem.*, 1947, **39**, 378.
[2] Désirant, *Bull. Acad. roy. Belg.*, 1955, **41**, 759.
[3] Godsell, Stacey, and Tatlow, *Nature*, 1956, **178**, 199.

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Like Wall *et al.*,[4] we have used Désirant's method and find it well suited to continuous preparation of hexafluorobenzene. Carbon tetrabromide, readily prepared from acetone,[5] was converted by activated antimony trifluoride into tribromofluoromethane in 65—75% yield. Pyrolysis at atmospheric pressure in a nickel tube lined with platinum gave readily-reproducible results leading to the establishment of optimum conditions. The pyrolysis was catalysed by platinum gauze; nickel tubes or nickel packings were much less effective than platinum. Under optimum conditions the conversion into hexafluorobenzene was 35% with a 48% net yield.

The formation of hexafluorobenzene by pyrolysis of tribromofluoromethane probably involves difluoroacetylene as intermediate ($CFBr_3 \longrightarrow CFBr_2{\cdot}CFBr_2 \longrightarrow C_2F_2 \longrightarrow C_6F_6$); it is well known that dichloroacetylene trimerises to hexachlorobenzene.[6]

Hexafluorobenzene, like other perfluoro-olefins, is sensitive towards nucleophilic attack, but only in a non-aqueous solvent. Thus hexafluorobenzene is resistant to aqueous sodium hydroxide at atmospheric pressure, and although reaction occurs under autogenous pressure, pentafluorophenol is produced in low yield, if at all. This contrasts with hexachlorobenzene which gives pentachlorophenol in 80% yield under similar conditions.[7] Similarly, methanolic sodium hydroxide converts hexachlorobenzene into pentachlorophenol in 99% yield,[8] whereas hexafluorobenzene under comparable conditions in ethanol reacts only slowly and yields 2 : 3 : 4 : 5 : 6-pentafluorophenetole. The apparent ease of nucleophilic attack by ethoxide ion is confirmed by the ready conversion of hexafluorobenzene into 2 : 3 : 4 : 5 : 6-pentafluorophenetole by ethanolic potassium ethoxide; small amounts of ethoxide ion are known to be present in ethanolic potassium hydroxide.

Pentafluorophenol was prepared in good yield under mild conditions by heating hexafluorobenzene with potassium hydroxide in *tert.*-butyl alcohol. The phenol has a typical phenolic odour and, as expected, is markedly acidic. Pentafluorophenol has a b. p. (143°) much lower than that of phenol (182°), indicating a decrease in intermolecular hydrogen bonding accompanied by some intramolecular hydrogen bonding (see discussion of infrared spectra below).

It readily forms a crystalline potassium salt and yields such crystalline esters as benzoate and 3 : 5-dinitrobenzoate without difficulty.

Infrared Spectra of Pentafluorophenyl Derivatives.—An interesting point is whether hexafluorobenzene shows aromatic character with full conjugation of the three double

TABLE 1.

		Ring vibration ($cm.^{-1}$)	C–F stretching vibrations ($cm.^{-1}$)
C_6F_6	Vap.†	1536	1021, 1003
,,	Liq.	1531	1018, 994
$C_6F_5{\cdot}OEt$	Liq. film	1515	1037, 997
$C_6F_5{\cdot}OH$	Liq. film	1515, 1534 (doublet)	1016, 996, 979
,,	Vap.	1522, 1543 (doublet)	1016, 994, 978
$C_6F_5{\cdot}OK$	Mull *	1479, 1497	1009, 974
$C_6F_5{\cdot}O{\cdot}COPh$	Mull *	1520	1044, 1024, 1009, 996
$C_6F_5{\cdot}O{\cdot}CO{\cdot}C_6H_3(NO_2)_2$	Mull *	1524	1014, 995

* In Nujol or hexachlorobutadiene.

† Delbouille, *J. Chem. Phys.*, 1956, **25**, 182, reports bands at 1529, 1018, and 1003 $cm.^{-1}$ for a sample prepared by Désirant.

bonds. Hexafluorobuta-1 : 3-diene, for example, is quite different from buta-1 : 3-diene; its chemical reactivity and its infrared spectrum show that there is little conjugation

[4] Hellmann, Peters, Pummer, and Wall, *J. Amer. Chem. Soc.*, 1957, **79**, 5654.

[5] Hunter and Edgar, *ibid.*, 1932, **54**, 2025; Berthelot and Jungfleisch, *Annalen*, 1870, *Supplement*, **7**, 252.

[6] Nicodemus, *J. prakt. Chem.*, 1911, **83**, 312; Ott and Dittus, *Ber.*, 1943, **76**, 80; Goodall and Howlett, *J.*, 1954, 2599.

[7] Troitskii and Voronina, *Org. Chem. Ind.* (*U.S.S.R.*), 1940, **7**, 240.

[8] Smith and Livak, U.S.P. 2,107,650/1938; *Chem. Abs.*, 1938, **32**, 2548.

between the double bonds.[9] Examination of the infrared spectra of hexafluorobenzene and its derivatives strongly indicates aromatic character in the cyclic triene system. All the spectra show strong C–F stretching bands near 1000 cm.$^{-1}$, and another strong band near 1520 cm.$^{-1}$ (Table 1) that is attributed to the C:C ring vibration. The extent of conjugation is revealed by comparison with other C:C stretching vibrations, shown in Table 2, which are at much higher frequency.

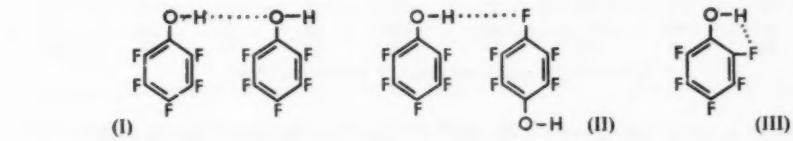
TABLE 2. C:C *Stretching vibration* (*cm.*$^{-1}$).

cis–trans-HCF:CFH...	*a*	Vap.	1736, 1715	CF_2·CF:CF·CF_2	*e*	Vap.	1802
cis-CF_3·CF:CF·CF_3 ...	*b*	Vap.	1733	CF_2·CF_2·CF:CF·CF_2·CF_2	*f*	Vap.	1754
cis-C_2F_5·CF:CF·C_2F_5	*c*	Vap.	1712	CF_2·CF:CF·CF_2·CF:CF ...	*g*	CCl_4 Soln.	1739
CF_2:CF·CF:CF_2	*d*	Vap.	1770	CF_2·CF_2·CF:CF·CF:CF	*g*	CCl_4 Soln.	1754, 1712

[a] Haszeldine and Steele, *J.*, 1957, 2800. [b] Haszeldine, *J.*, 1952, 4423. [c] Haszeldine and Steele, *J.*, 1953, 1592. [d] Haszeldine, *J.*, 1952, 4423. [e] Unpublished work. [f] Haszeldine, *Nature*, 1951, **168**, 1028. [g] Evans and Tatlow, *J.*, 1954, 3779; 1955, 1184.

The ring vibration of the pentafluorophenoxide ion at 1502 cm.$^{-1}$ is at lower frequency than that in the covalent pentafluorophenyl derivatives, indicating increased resonance of type shown inset.

The spectrum of pentafluorophenol in the 3500 cm.$^{-1}$ region was studied in more detail to determine the effect of hydrogen bonding. The liquid film shows a sharp band at 3571 cm.$^{-1}$ and a broad band of approximately equal intensity centred on 3425 cm.$^{-1}$; the former is the typical "free" hydroxyl stretching vibration band and the latter the typical hydrogen-bonded hydroxyl group band. The spectrum of pentafluorophenol vapour shows a sharp strong band at 3623 cm.$^{-1}$ and no band in the 3400 cm.$^{-1}$ region. A 1% solution in carbon tetrachloride shows a single sharp band at 3571 cm.$^{-1}$ with a weak shoulder at 3676 cm.$^{-1}$ and a weak broad bonded hydroxyl band at 3257 cm.$^{-1}$. These facts show that intermolecular hydrogen bonding of type (I) [or, less likely, (II)] occurs in the liquid, and is absent from the vapour and much reduced in solution



(I) (II) (III)

in a non-polar solvent. The situation is similar to that found with perfluoroalkyl alcohols[10] where the decreased basicity of the oxygen caused by the adjacent electron-attracting fluorocarbon group decreases its participation in intermolecular hydrogen bonding. Judged by the relative intensities of the "bonded" and "free" hydroxyl group bands, intermolecular hydrogen bonding is weaker in pentafluorophenol than in phenol. As with the perfluoro- and perchloro-alcohols, intramolecular hydrogen bonding of type (III) is possible, and the band at 3623 cm.$^{-1}$ could be ascribed to a "free" hydroxyl group appearing again at 3676 cm.$^{-1}$ in the solution, with the 3571 cm.$^{-1}$ band caused by bonding of type (III). Alternatively, the shift from 3623 to 3571 cm.$^{-1}$ is to be ascribed to the dielectric constant of the medium. The marked difference in b. p. between phenol and pentafluorophenol

[9] Haszeldine, *J.*, 1952, 4423.
[10] *Idem*, *J.*, 1953, 1757.

is caused by decrease in intermolecular hydrogen bonding rather than by increase in intramolecular hydrogen bonding, *i.e.*, the change in basicity of the oxygen atom is responsible rather than the presence of fluorine in the *ortho* position to give structures of type (III); the difference in b. p. between *o*-fluorophenol (152°) and *p*-fluorophenol (189°) is to be explained similarly.

Experimental

Preparation of Tribromofluoromethane.—Dry carbon tetrabromide (1 mole), antimony trifluoride (0·5 mole), and bromine (0·05 mole) were heated to 120—130° during 1 hr. so that the tribromofluoromethane distilled out as it was formed. The temperature was later raised to 150—160° for 0·5 hr. to ensure complete removal of the product. The crude product was washed with 5% aqueous tartaric acid, 10% aqueous sodium sulphite, 2% aqueous sodium hydroxide, and water; it was then dried (P_4O_{10}) and distilled to give tribromofluoromethane (65—75%), b. p. 106—107°. Dibromodifluoromethane, b. p. 23·5°, was also formed (5—10%). Rathsburg [11] obtained a 19% yield of tribromofluoromethane by this method.

Preparation of Hexafluorobenzene.—The pyrolysis apparatus consisted of a tube of platinum foil (50 cm. long × 1·8 cm. i.d.), encased in nickel, and heated electrically over 40 cm. of its length. The nickel inlet and outlet tubes were water cooled by means of lead coils. The tube was packed with a 3 in. square of platinum gauze of 80-mesh 0·003 in. diameter wire. Under optimum conditions, tribromofluoromethane (130 g./hr.) was dripped at constant rate into the furnace at 630—640°; nitrogen (60 ml./hr.) was added simultaneously. The apparatus was operated continuously. The products, condensed in two cooled traps, were washed with ice-cold 10% aqueous sodium sulphite, aqueous 5N-sodium hydroxide, and water, then dried (P_4O_{10}) and distilled through a Podbielniak column of 25—30 plates to give hexafluorobenzene (35%; 48% on tribromofluoromethane actually used) (Found: C, 38·8%; *M*, 187. Calc. for C_6F_6: C, 38·7%; *M*, 186), b. p. 80—81°, n_D^{20} 1·3777, which solidified at 0°. Under these conditions some tribromofluoromethane (26%) was recovered, and 65% of the theoretical amount of bromine was liberated. Investigation of the products of b. p. > 110° (20 g./hr. on the above scale) will be described later. With apparatus of the dimensions stated, higher rates of flow left much tribromofluoromethane unchanged whereas lower rates gave more by-products. Typical results at 640° are shown in the annexed Table.

$CFBr_3$, g./hr.	Br liberd. %	$CFBr_3$ recd. %	C_6F_6 Yield %	C_6F_6 Net yield %	$CFBr_3$, g./hr.	Br liberd. %	$CFBr_3$ recd. %	C_6F_6 Yield %	C_6F_6 Net yield %
72·5 *	74	23	28	36	130 †	88	11	33	37
101 *	70	24	28	37	170	54	41	26	44
310	45	50	21	42	130	60	27	34	47
530	26	66	13	37	130	65	26	35	48

* Tube without gauze packing. † Furnace at 680°.

Pyrolysis in a nickel tube gave a 25% yield of hexafluorobenzene; use of nickel wire as packing reduced the yield substantially.

The purity of the hexafluorobenzene is shown by gas chromatography, analysis, molecular-weight determination, and infrared spectroscopy. The infrared bands reported by Stacey *et al.*[3] at 1702, 1761, and 1802 cm.$^{-1}$ were not present in our material, and must be attributed to impurity.

Action of Aqueous Sodium Hydroxide on Hexafluorobenzene.—The action of aqueous sodium hydroxide on hexafluorobenzene was studied at atmospheric pressure and in an autoclave; the conditions of concentration, temperature, reactant ratios, etc., were varied. Hexafluorobenzene was resistant to attack by aqueous alkali at atmospheric pressure; reaction occurred at higher pressures but gave no readily identifiable product.

2 : 3 : 4 : 5 : 6-*Pentafluorophenetole.*—Hexafluorobenzene (5·0 g.) was heated under reflux with N-potassium ethoxide in anhydrous ethanol (25 ml.) for 1 hr. The mixture was poured into an excess of water and the organic layer was washed with water, dried, and distilled to give

[11] Rathsburg, *Ber.*, 1918, **51**, 669.

hexafluorobenzene (1·1 g., 22%) and 2 : 3 : 4 : 5 : 6-*pentafluorophenetole* (3·2 g., 56%) (Found: C, 45·1; H, 2·5%. $C_8H_5OF_5$ requires C, 45·3; H, 2·4%), b. p. 152—153°, n_D^{20} 1·4109.

Action of Ethanolic Potassium Hydroxide on Hexafluorobenzene.—Hexafluorobenzene (2·0 g.) and 10% ethanolic potassium hydroxide (10 ml.) were heated in a sealed tube at 120° for 30 min.; the mixture was poured into water. The dried ($MgSO_4$) ether extract was distilled to give hexafluorobenzene (0·9 g., 45%) and 2 : 3 : 4 : 5 : 6-pentafluorophenetole (1·1 g.; 48%), identical with the compound described above.

Pentafluorophenol.—Hexafluorobenzene (10·0 g.; 0·054 mole), potassium hydroxide (7·6 g.; 0·135 mole), and *tert.*-butyl alcohol (100 ml.; 1·1 moles) were heated under reflux for 1 hr. Water (200 ml.) was added to the cooled reactants and the *tert.*-butyl alcohol distilled off. The residual aqueous solution was filtered and extracted with ether (2 × 50 ml.). The aqueous layer was then acidified with 5N-hydrochloric acid (80 ml.), a colourless oil separating. This was extracted with ether (4 × 50 ml.), and the ethereal layer washed with water, dried ($MgSO_4$), and distilled to give *pentafluorophenol* (7·0 g.; 71%) (Found: C, 39·3; H, 0·9%; equiv., 183·6. C_6HOF_5 requires C, 39·1; H, 0·5%; equiv., 184·1), m. p. 25—30°, b. p. 143°, n_D^{20} 1·4270. It proved difficult to dry ethereal pentafluorophenol thoroughly, and analysis for hydrogen was carried out after the distilled liquid had been dried by azeotropic distillation with benzene immediately before analysis. The equivalent weight was determined by titration in ethanolic solution against standard sodium hydroxide with phenolphthalein as indicator.

Pentafluorophenol, a crystalline solid with marked phenolic odour, gives a deep violet colour with aqueous ferric chloride and liberates carbon dioxide from cold aqueous sodium hydrogen carbonate. It is hygroscopic but not freely soluble in water.

Potassium Pentafluorophenoxide.—Hexafluorobenzene (2·0 g.) was heated under reflux with potassium hydroxide (1·5 g.) in *tert.*-butyl alcohol (20 ml.) for 1 hr. An excess of water was added and the alcohol was distilled off. The residual aqueous solution was filtered and cooled, white needles were deposited of *potassium pentafluorophenoxide* (1·5 g.; 69%) (Found: C, 32·2; H, 0·2. C_6OF_5K requires C, 32·4; H, 0%), m. p. 246° (slight decomp.) (from water); it is hygroscopic, soluble in acetone, but insoluble in ether. Potassium pentachlorophenoxide, similarly prepared, deposits pentachlorophenol as a solid when its aqueous solution is acidified.[12]

Pentafluorophenyl Benzoate and 3 : 5-*Dinitrobenzoate.*—These were prepared by treatment of pentafluorophenol in pyridine with the appropriate acid chloride. The *benzoate* (Found: C, 52·4; H, 1·7. $C_{13}H_5O_2F_5$ requires C, 54·2; H, 1·7%) crystallised from aqueous ethanol as white needles, m. p. 74—75°; it shows carbonyl absorption in the infrared at 1773 cm.$^{-1}$.

The 3 : 5-*dinitrobenzoate* (Found: C, 41·5; H, 0·8; N, 7·4. $C_{13}H_3O_6N_2F_5$ requires C, 41·3; H, 0·8; N, 7·4%) crystallised from light petroleum as plates, m. p. 107°; its carbonyl absorption is at 1776 cm.$^{-1}$.

The authors thank Mlle. Y. Désirant for providing details of her method for preparing hexafluorobenzene. One of them (J. M. B.) is indebted to the D.S.I.R. for a Research Studentship.

MANCHESTER COLLEGE OF SCIENCE AND TECHNOLOGY. [*Received, June 16th*, 1958.]

[12] Bartlett, U.S.P. 2,644,015/1953; *Chem. Abs.*, 1954, **48**, 5216.

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5. *The Chromatography of Gases and Vapours. Part VI.* Use of the Stearates of Bivalent Manganese, Cobalt, Nickel, Copper, and Zinc as Column Liquids in Gas Chromatography.*

By D. W. Barber, C. S. G. Phillips, G. F. Tusa, and A. Verdin.

A series of retention times have been measured by use of gas–liquid chromatographic columns, in which the column liquids are molten stearates of manganese, cobalt, nickel, copper, or zinc. The behaviour of these columns towards different classes of vapour is compared with that of a more conventional column in which liquid Apiezon grease L is used. Particularly strong interactions have been found between amines and the metal salts.

The use of metal salts in gas–liquid chromatographic columns is of interest as a possible means of obtaining selective separations as a result of interaction between vapours and the metal atoms. This was first demonstrated by Bradford, Harvey, and Chalkley [1] who used a solution of silver nitrate in ethylene glycol to achieve selective retardation of unsaturated hydrocarbons. We have used metal stearates at 156°, a temperature at which they are all liquid, but such systems may also serve as a model for the behaviour of purely inorganic salts which will probably be the most suitable liquid phases at column temperatures above 500°. The results obtained with the metal stearate columns may also be of interest as illustrating a method which may be useful for studying complex formation. For this reason we have chosen a group of metals whose aqueous complex-ion chemistry has been much studied.

Experimental

The column material was packed into a glass tube of 4 mm. in. diam., 100 cm. long. The column temperature was controlled by a vapour jacket. Nitrogen–hydrogen (1 : 3 v/v), used as carrier gas, was preheated before entering the column. The sample was introduced to the column by Scott's capillary method.[2] The chromatograms were recorded with a hydrogen-flame detector,[2] the output being fed from the thermocouple to a milliammeter recorder *via* a D.C. microvoltmeter (Pye, Cambridge). Gas flow-rate was measured on a soap-bubble flowmeter, corrections being made for the water vapour pressure of the soap solution.

Metal stearates, prepared by double decomposition, were supplied by the Watford Chemical Company, and contained up to 2% of sodium chloride. The cobalt salt was hydrated. The water was removed either by heating alone or in benzene solution. All values quoted in this paper are for the anhydrous salt. A sample of ferrous stearate was prepared but as this rapidly oxidised in contact with even small traces of air, it was not thought to be satisfactory as a column liquid. The manganese stearate was found to oxidise when heated in air at 160°. No stearate had a sharp m. p., but they softened gradually over about 5°. Clear liquids were obtained at the following temperatures: Mn 104°, Co 92°, Ni 146°, Cu 101°, Zn 122°. Apiezon L high-vacuum grease was supplied by W. Edwards and Co.

The stearate column liquids (19 parts) or Apiezon L (25 parts) were mixed with Celite (100 parts), a solvent which was evaporated off with continuous stirring being used. Suitable solvents were ether for Apiezon L, and benzene for all stearates except that of nickel, for which *cyclo*hexylamine was suitable although it took many hours to remove.

The results given are derived from a large number of individual experiments. In order to check the stability of the columns and their reproducibility when packed in different ways and by different experimenters it was necessary to follow many separate runs, each containing one compound plus the internal standard (mesitylene) to avoid errors arising from competition for sites round the metal atoms. Thus Fig. 1 represents some 70 runs on the stearate and 50 on the Apiezon, similar work being done for the other stearates; for zinc stearate the experiments were repeated in a metal tube. The copper stearate column had to be

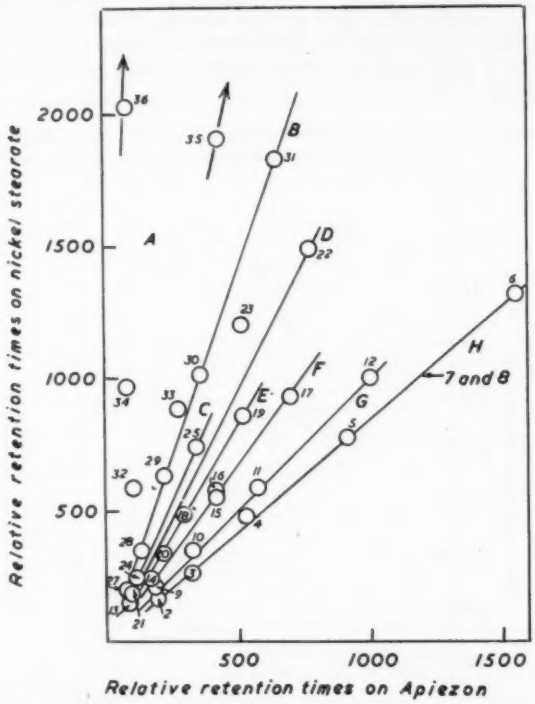
* Part V, *J.*, 1955, 1480.

[1] Bradford, Harvey, and Chalkley, *J. Inst. Petrol.*, 1955, **41**, 80.
[2] Scott, "Vapour Phase Chromatography," ed Desty, Butterworths, London, 1957, p. 131.

XUM

remade frequently owing to its decomposition by certain vapours. Each point in Fig. 2 represents some 20 experiments. In addition, for each amine it was necessary (on one metal stearate column) to make a number of experiments to correct for the asymmetry of the peaks.

FIG. 1. *Relative retention times on nickel stearate and on Apiezon at* 156°.



1 Hexane, 2 heptane, 3 octane, 4 nonane, 5 decane, 6 undecane, 7 dodecane, 8 tetradecane, 9 benzene, 10 toluene, 11 *m*-xylene, 12 mesitylene, 13 ethyl methyl ketone, 14 diethyl ketone, 15 butyl ethyl ketone, 16 methyl pentyl ketone, 17 hexyl methyl ketone, 18 *cyclo*pentanone, 19 *cyclo*hexanone, 20 1 : 1′-dimethylbutanol, 21 1-methylpropanol, 22 1-methylheptanol, 23 *cyclo*hexanol, 24 2-methylpropanol, 25 2-methylpentanol, 26 2-methylheptanol, 27 propanol, 28 butanol, 29 pentanol, 30 hexanol, 31 heptanol, 32 diethylamine, 33 dipropylamine, 34 *tert.*-butylamine, 35 aniline, 36 pyridine.

A, Amines; *B*, normal primary alcohols; *C*, 2-methyl alcohols; *D*, secondary alcohols; *E*, cyclic ketones; *F*, aliphatic ketones; *G*, aromatic hydrocarbons; *H*, aliphatic hydrocarbons; *I*, tertiary alcohols.

The point for 36 is 8073, 296; for 35 is 3811, 855; for 7 is 2205, 2670; and for 8 is 6290, 7775. The last two lie on line *H*, the first two in the direction of the arrows.

RESULTS

Relative retention times at 156° were measured with mesitylene as internal standard (retention time taken as 1000). From these, plots were made as in Fig. 1 of relative retention times on metal stearate against relative retention times on Apiezon L. Each homologous series gives a good straight line passing through the origin, indicating that for each series there is a constant difference of free energy of solution between metal stearate and the Apiezon. The gradients of the lines measure the retardations (relative to mesitylene) of substances when passed through a metal stearate instead of Apiezon. They may thus be called retardation factors. Similar plots were obtained for all the metals, so that it is only necessary to report the retardation factors for the various homologous series, as

in Fig. 2. There is a maximum at nickel stearate and a minimum at copper stearate for all the series plotted. Such a pattern is strongly reminiscent of that obtained for complex stabilities for substitution at the fifth and sixth positions as found in studies of the metal ions in aqueous solution, where the effect has been interpreted in terms of ligand-field theory.[3] In each homologous series, as with other column liquids, the logarithms of the retention times give straight lines when plotted against the number of carbon atoms.

Very much stronger retardations are found when amines are passed through the metal-salt columns. Table 1 gives a set of relative retention times for manganese stearate where the effect is relatively small.

FIG. 2. *Retardation factors for different metal stearates at* 156° (*curves lettered as for Fig.* 1).

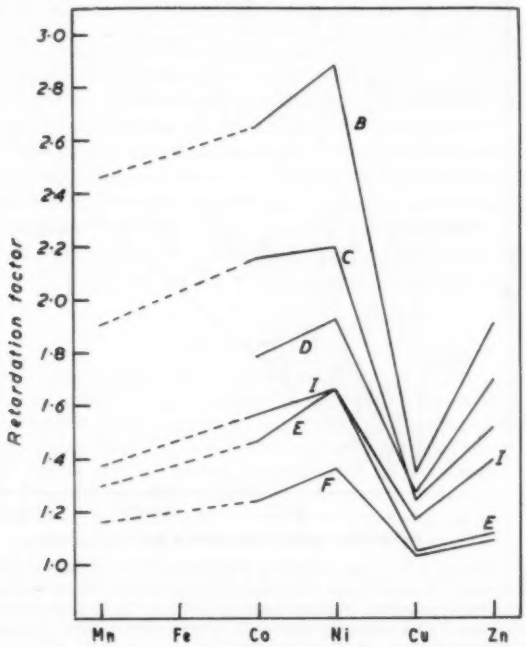


TABLE 1. *Relative retention times for amines on Apiezon L and on manganese stearate columns at* 156°.

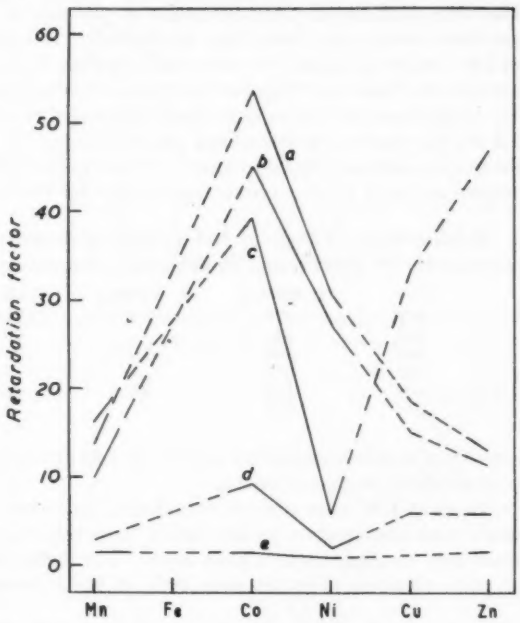
	Apiezon	Stearate		Apiezon	Stearate		Apiezon	Stearate
	Primary			Secondary			Tertiary	
Pr^i	66	2304	Et_2	99	1610	Et_3	187	328
Pr^n	173	3655	Pr^n_2	276	2134	Pr^n_3	619	649*
Bu^n	215	6032	Bu^n_2	758	4871	Bu^n_3	2382	3342
Bu^t	79	1550						
			Aromatic amines					
Aniline	855	2084	α-Picoline	416	1230	2 : 6-Lutidine	571	661
NN-Dimethylaniline	1835	1989	β-Picoline	535	7460	Pyrrole	202	301
Pyridine	296	3016	γ-Picoline	540	9670			

It has not yet been possible to obtain satisfactory results with primary amines for all the metal salt columns, but the general trends observed for the less strongly complexed amines are shown in Fig. 3. Accurate relative retention times for amines are difficult to

[3] Griffith and Orgel, *Quart. Rev.*, 1957, **11**, 387.

measure because of the markedly asymmetric peaks (sharp fronts and diffuse tails) which result when any but very small samples are used. Thus, with pyridine, symmetrical peaks only occur with samples less than 0·1 μl. The values quoted have been obtained either by using samples small enough to give symmetrical peaks, or by measuring from the back of the peak (the position of which remains constant with change of sample size) a distance equal to half the peak width for a non-complexed substance with a similar retention time. The latter method is naturally subject to an error which may amount to 2—3%, but in the cases where results have been obtained by both methods they agree very well. The sharp fronts and diffuse tails are presumably associated with competition among the amine molecules for sites, or the more favoured sites around the metal atoms.

FIG. 3. *Retardation factors for different metal stearates at* 156°.



a, β-Picoline; *b*, pyridine; *c*, diethylamine; *d*, α-picoline; *e*, tributylamine.

With copper stearate both the shapes and relative retention times of amine peaks have been found to vary curiously with flow-rate. This is particularly so at flow rates greater than 20 c.c./min., and may be connected with some slow complexing process. The results plotted for copper stearate in Fig. 3 are for low flow-rates and for the normal sharp-fronted type of amine peak, but they have been marked by a broken line to indicate that there is some uncertainty attached to them. Primary amines decomposed the copper stearate column.

Retardation factors for secondary and tertiary amines with Mn, Co, and Zn stearates were proportional to the basic dissociation constants of the amines. This relationship did not apply to primary amines or pyridine homologues, where the retardation factors are relatively much greater (except for α-substituted pyridines). For the primary amines there may perhaps be some effect involving hydrogen bonding of the amine to the stearate groups around the metal atom. For pyridine and β- and γ-picoline there is presumably some π-bonding from the metal which is absent from bonding to a proton. α-Picoline

and 2 : 6-lutidine are very little retarded by the metal stearates, which suggests that there is steric interference from the methyl groups adjacent to the pyridine-nitrogen atom.

The results for the series diethylamine, dipropylamine, and dibutylamine are peculiar in that while the change is regular (by a factor of 2·8) along the series on Apiezon, this is not so on the metal salts. There is a somewhat similar phenomenon in tertiary amines.

The changes for the amines along the series of metals are difficult to understand in terms of simple complex-ion theory. The marked drop from cobalt to nickel stearate which is the particularly strange feature of the series may perhaps be correlated with some peculiarity of structure in nickel stearate, whose m. p. is greater than those of the other members of the series. A few results obtained with nickel oleate as column liquid suggest that here complexing and retardation of amines may be stronger than with cobalt stearate. Nickel oleate liquefies between 25° and 30°.

The special interactions with metal stearates make it possible to use these column liquids to effect separations which may otherwise be difficult. A suitable column for a specific separation at 156° can be deduced from the results in Figs. 1, 2, and 3 and Table 1, but for illustration we quote in Table 2 a few instances of pairs of substances which happen to be difficult to separate on Apiezon but can be quite easily separated on manganese stearate. Also given in Table 2 are the number of theoretical plates required for 99·9% separation, as estimated from the graph published by Glueckauf.[4] These values will only apply when sufficiently small samples are used to give symmetrical peaks for the amines.

TABLE 2. *Relative retention times (t) and numbers of theoretical plates (n) for separations on Apiezon and on manganese stearate columns.*

Compound	B. p.	*t*, Apiezon	*n*, Apiezon	*t*, Mn Ste.	*n*, Mn Ste.
β-Picoline	143°	535	400,000	7460	600
γ-Picoline	143	540	—	9670	—
γ-Picoline	143	540	15,000	9670	5
2 : 6-Lutidine	143	571	—	773	—
n-Butyl alcohol	118	123	4000	356	250
*iso*Butyl alcohol	108	111	—	244	—

The marked selectivity of metal stearates for certain specific groups might also be used to identify the class to which a compound belongs.

Relative retention times at 156° were reproducible during up to two months of column use. Some experiments with zinc stearate packed into a brass tube showed that the same relative retention times were obtained as in a glass tube. The metal stearate columns as used had theoretical plate numbers approximately 60% of those found for the Apiezon column.

Thermodynamic Data.—Specific retention volumes,[5] V_g (previously called corrected retention volumes per gram [6]), were obtained for mesitylene, the internal standard, at 156° and at 110·6°, by Littlewood, Phillips, and Price's procedure.[6] The values were V_g (156°) 68·1, V_g (110·6°) 241·4. The density of cobalt stearate (ρ) at 156° was 0·902 g./c.c. A series of relative retention times were measured on cobalt stearate at 110·6°. From these results free energies, heats, and entropies of solution were calculated by use of the relations

$$-\Delta G = \boldsymbol{R}T \ln \alpha$$

$$\alpha = \frac{\text{Weight of vapour per unit volume of column liquid}}{\text{Weight of vapour per unit volume of gas}}$$

$$V_g = 273\alpha/T\rho$$

$$\mathrm{d} \ln V_g/\mathrm{d}T = \Delta H/\boldsymbol{R}T^2$$

$$\Delta G = \Delta H - T\Delta S$$

[4] Glueckauf, *Trans. Faraday Soc.*, 1955, **51**, 34.
[5] Ambrose, Keulemans, and Purnell, *Analyt. Chem.*, 1958, **30**, 1582.
[6] Littlewood, Phillips, and Price, *J.*, 1955, 1480.

FIG. 4. *Heats of solution in cobalt stearate (kcal./mole). (For key see Fig. 1.)*

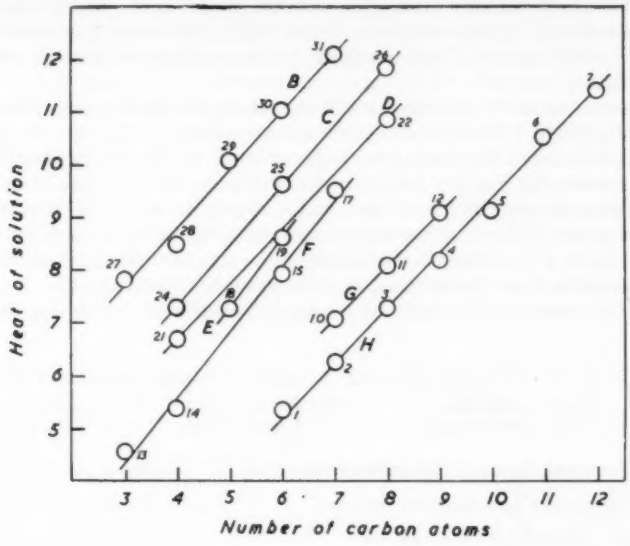
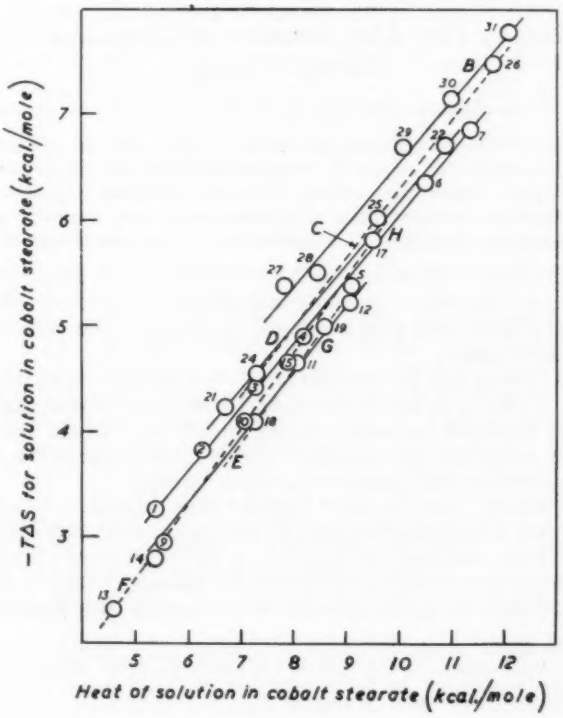


FIG. 5. *Relation between heats and entropies of solution in cobalt stearate. (For key see Fig. 1.)*



In calculating the entropies the approximation was made that the heat of solution at 156° was the same as the mean heat of solution over the range 110·6—156°. The free energies, heats, and entropies of solution will correspond to the transfer of 1 mole of the vapour to the solution in cobalt stearate from a volume in the gas phase which is the same as it will occupy in solution.

In each case a constant increment was found along any homologous series in ΔG, ΔH, and ΔS per CH_2 group. Some heats of solution are plotted in Fig. 4. As has been noted in other solution studies,[7] there was a fairly linear relation between the heats and entropies of solution, as shown by Fig. 5. Excess heats of solution were calculated for some hydrocarbons and alcohols using heats of vaporisation extrapolated to 133° (mean of 110·6° and 156°) from values in Tables.[8] They were between 0·6 and 1·1 kcal./mole for hydrocarbons and of the order of 2 kcal./mole for alcohols, these values corresponding in each case to endothermic transfer from the pure solute to solution in cobalt stearate.

Some activity coefficients calculated for typical solutes in cobalt stearate at 156° are in Table 3.

TABLE 3. *Activity coefficients for solution in cobalt stearate at* 156°

Heptane	0·88	*m*-Xylene	0·59	Butyl alcohol ...	0·33	Diethylamine...	0·011
Octane	0·80	Mesitylene	0·55	Pentyl alcohol ...	0·41	Triethylamine	0·15

We thank Imperial Chemical Industries Limited for the loan of recorders.

INORGANIC CHEMISTRY LABORATORY, OXFORD. [*Received, July* 18*th*, 1958.]

[7] Bell, *Trans. Faraday Soc.*, 1937, **33**, 496.
[8] International Critical Tables.

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6. *Allenes. Part II.*[1] *Reactions of Prop-2-yn-1-ols with Thionyl Chloride.*

By Y. R. BHATIA, PHYLLIS D. LANDOR, and S. R. LANDOR.

Tertiary acetylenic carbinols are shown to react with thionyl chloride to give 1-chloroallenes and alkenynes, whereas secondary and primary acetylenic carbinols give mainly the normal acetylenic chlorides. Good yields of chloroallenes are obtained from α-polysubstituted and sterically hindered tertiary acetylenic carbinols. The mechanism of these reactions is discussed.

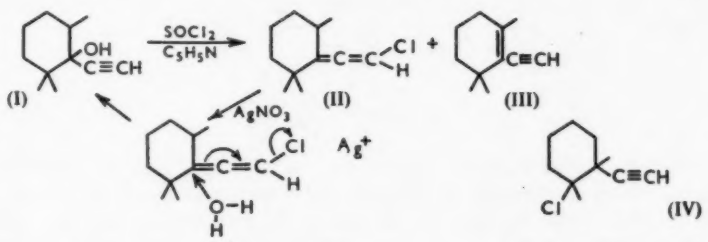
IT has been shown [1] that pyrolysis of prop-2-ynyl acetates yields allenic acetates, probably through a cyclic transition state. A similar mechanism might afford allenic chlorides by reaction of thionyl chloride with prop-2-yn-1-ols, the unstable chlorosulphite being formed as a short-lived intermediate.

The literature showed that the products from this reaction could roughly be divided into two classes: (*a*) the expected 3-chloroprop-1-ynes [2] and (*b*) rearrangement products, often inadequately identified, for which varying structures had been put forward. Since the latter products might well have contained allenic halides some of this earlier work was repeated and the products were examined for allenic groups.

For instance, Sobotka and Chanley [3] reported that treatment of 1-ethynyl-2 : 2 : 6-trimethyl*cyclo*hexanol with thionyl chloride in the presence of excess of pyridine gave a 54% yield of a chlorine-containing compound (b. p. 96°/14 mm., n_D^{20} 1·5030) which was not the expected 1-ethynyl-2 : 2 : 6-trimethyl*cyclo*hexyl chloride. They rejected an allenic structure for this compound on the grounds of its reaction with alcoholic silver nitrate

[1] Part I, *J.*, 1956, 1015.
[2] *E.g.*, Hennion and Sheehan, *J. Amer. Chem. Soc.*, 1949, **71**, 1964; Bailey and Fujuwara, *ibid.*, 1955, **77**, 165.
[3] Sobotka and Chanley, *ibid.*, 1949, **71**, 4136.

and suggested structure (IV), resulting from Wagner–Meerwein rearrangement of a prop-1-ynyl carbonium ion. In our hands comparable conditions to those used by Sobotka and Chanley gave a 60% yield of a chloride with similar physical constants, as well as some 1-ethynyl-2 : 6 : 6-trimethyl*cyclo*hexene (III). A strong allene C=C stretching band at 1950 cm.$^{-1}$ as well as an exceptionally intense band at 730 cm.$^{-1}$ (cf. C–Cl stretching for vinyl chloride [4]) showed the presence of an allenic chloride (II), which was corroborated by the absence of any acetylenic CH stretching band from the 3300 cm.$^{-1}$ region and of any maximum from the ultraviolet spectrum. No immediate reaction was observed with alcoholic silver nitrate but prolonged heating gave over 90% of the theoretical quantity of silver chloride. The organic material isolated consisted mainly of an acetylenic carbinol (as shown by the infrared spectrum) similar in properties to the original carbinol, but the quantities obtained were insufficient for rigorous identification. A mechanism can be put forward in which a S_N2' attack by a water molecule follows co-ordination of the chlorine with the silver ion, giving the original acetylenic carbinol (I): removal of the halide ion



is facilitated by the ready access of the terminal carbon atom to the π-electrons of the 2 : 3-double bond of the allene, making it more reactive than a normal vinyl chloride.

Hurd and Jones,[5] treating ethynyl*cyclo*hexanol in pyridine with thionyl chloride at 50—60°, obtained an inert chloride which was sufficiently identified as 1-1′-chlorovinyl-*cyclo*hexene, probably formed from ethynyl*cyclo*hexene (which was also isolated) by addition of hydrogen chloride. We repeated this reaction at 0° and −80° as at these temperatures pyridine hydrochloride would be unlikely to react with the acetylene group. The product was mainly ethynyl*cyclo*hexene, but it contained up to 25% of allenic chloride as shown by the infrared spectra. Separation was achieved by treating the mixture with alcoholic silver acetate, which removes the ethynyl compounds as their silver salts but leaves the allenic chloride largely unaffected; it does, however, introduce a small amount of carbonyl-containing impurity into the product.

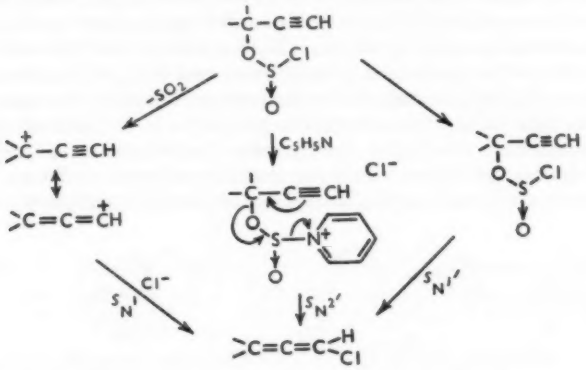
1-Ethynyl-2 : 2 : 6 : 6-tetramethyl*cyclo*hexanol, which cannot give the corresponding ethynyl*cyclo*hexene, gave an 83% yield of allenic chloride. Similarly, in the aliphatic field, 3-*tert.*-butyl-4 : 4-dimethylpent-1-yn-3-ol gave 3-*tert.*-butyl-1-chloro-4 : 4-dimethylpenta-1 : 2-diene in 74% yield; again no α-hydrogen atom is available for elimination.

The same experimental conditions gave (*a*) 25% of 1-chloro-4-methyl-3-*iso*propylpenta-1 : 2-diene from 4-methyl-3-*iso*propylpent-1-yn-3-ol, and (*b*) 35% of 1-chloro-3 : 4 : 4-trimethylpenta-1 : 2-diene from 3 : 4 : 4-trimethylpent-1-yn-3-ol. Other tertiary ethynyl carbinols, *e.g.*, CH:C·CR_2·OH where R = Et, Pr^n, or Bu^i, gave approximately 10% of the corresponding 1-chloroallenes. The principal by-product isolated was alkenyne resulting from the indirect dehydration of the acetylenic carbinol. No acetylenic chlorides could by detected. It is evident that the proportion of alkenyne in the product increases as the number of α-hydrogen atoms increases and as the steric hindrance at those hydrogen atoms decreases.

The formation of allenic chlorides from sterically hindered tertiary ethynylcarbinols

[4] Thompson and Torkington, *Proc. Roy. Soc.*, 1945, *A*, **184**, 21; Torkington, *ibid.*, 1951, *A*, **206**, 17.
[5] Hurd and Jones, *J. Amer. Chem. Soc.*, 1934, **56**, 1924.

could be the result of an S_N1, S_N2', or S_Ni' reaction of the unstable, unisolatable chlorosulphite (as shown). No precise information is available regarding the mechanism of the reaction of thionyl chloride with tertiary alcohols. In the presence of excess of pyridine optically active secondary alcohols give chlorides with predominantly inverted configuration,[6] and allylic alcohols give mainly the unrearranged normal allylic chlorides,[7]



indicating an S_N2 type mechanism. By analogy an S_N2' mechanism would be expected to be responsible for the formation of allenic chlorides under these conditions. Clearly an S_Ni' mechanism would be more favourable to the formation of allenic halide and if realised should give higher yields. The best conditions for an S_Ni' mechanism are dilution in a nucleophilic solvent, such as ether or dioxan, and absence of an added base, such as pyridine.[8] Unfortunately, the reaction of tertiary alcohols in the absence of a base is very slow, particularly so when hindered ethynylcarbinols are used. Thus, 1-ethynyl-2 : 2 : 6-trimethyl*cyclo*hexan-1-ol was recovered substantially unchanged after reaction with thionyl chloride in dry ether at room temperature or under reflux. Reasonable yields of allenic chlorides, however, were obtained from most of these alcohols by raising the temperature of the reaction mixture either by evaporating most of the ether at the end of the experiment and heating the residue under reflux, or by the use of dry dioxan as solvent. Small quantities of rearranged products which could not be separated from the allenic chlorides by fractionation (as shown by the persistence of weak twin bands between 1600 and 1650 cm.$^{-1}$, absent in the pure allenic chloride) contaminated these allenes, and owed their formation to the acidic conditions developing during the experiment in the absence of pyridine. Less alkenyne was always isolated in the absence than in the presence of a base, suggesting a base-catalysed elimination mechanism of the *E*2 type for the formation of alkenyne in the presence of pyridine.

Reaction of secondary ethynylcarbinols (prepared from aldehydes) with thionyl chloride gave mainly the normal acetylenic chlorides. *E.g.*, hex-1-yn-3-ol gave 3-chlorohex-1-yne containing approximately 10% of the allenic chloride and the normal chloride obtained in dioxan contained about 20% of allene. Jacobs, Teach, and Weiss,[9] in work on the dehalogenation of allenic halides, claimed to have obtained a 44% yield of 1-chlorohexa-1 : 2-diene by using a mixture of diethyl and di*iso*propyl ether as solvent, but gave no further experimental details. 1-Phenylprop-2-yn-1-ol gave 3-chloro-3-phenylprop-1-yne in good yield, but no trace of allenic material was detected by infrared analysis. In this case the well-known stability of the benzyl carbonium ion suggests a S_N1 mechanism.

[6] Cowdrey, Hughes, Ingold, Masterman, and Scott, *J.*, 1937, 1252 and references quoted; Gerrard, *J.*, 1944, 85.
[7] De Wolfe and Young, *Chem. Rev.*, 1956, **56**, 753 and references quoted.
[8] Boozer and Lewis, *J. Amer. Chem. Soc.*, 1953, **75**, 3182.
[9] Jacobs, Teach, and Weiss, *ibid.*, 1955, **77**, 6254.

1-Chloroallenes have previously been prepared by the action of concentrated hydrochloric acid, in the presence of cuprous and ammonium chlorides, on 3-chloroacetylenes or directly on ethynylcarbinols.[9,10] After lengthy reactions the yields obtained by this method have been variable and in many instances infrared data were not available as a criterion of the purity of the allenic product.

Experimental

Ultraviolet spectra were determined for 95% EtOH ethanolic solutions by using a Unicam S.P. 500 spectrophotometer, and infrared spectra with a Hilger H 800 or a Grubb-Parsons instrument. The acetylenic alcohols were purified until there were no carbonyl bands in the infrared spectra.

2 : 2 : 6-*Trimethyl*cyclo*hexylidenevinyl Chloride* (II).—(*a*) 1-Ethynyl-2 : 2 : 6-trimethyl*cyclo*hexanol (8·3 g.) was mixed with dry redistilled pyridine (6 g.) and cooled in ice. Thionyl chloride (3·6 ml.) was added during 1 hr. with rapid stirring. The stirred mixture was allowed to warm to room temperature, pyridine hydrochloride filtered off, and the product washed with dilute hydrochloric acid, water, and aqueous sodium hydrogen carbonate, and distilled through a 6″ column of Fenske rings to give two main fractions; the first, b. p. 82°/15 mm., rapidly becoming pink in the air, was 1-ethynyl-2 : 6 : 6-trimethyl*cyclo*hexene (III) (1·4 g., 19%), $\lambda_{max.}$ 227 mμ (ε 11,000); the second, b. p. 92—94°/15 mm., n_D^{20} 1·4998, was **2 : 2 : 6-*trimethyl*cyclo*hexylidenevinyl chloride*** (II) (5·5 g., 60%), $\nu_{max.}$ 3275 w (trace C≡CH), 1950 m (C=C=C), and 730 s cm.$^{-1}$ (C=C=CHCl). Refractionation gave material of b. p. 96°/15 mm., n_D^{20} 1·5020 (Found: C, 72·6; H, 9·7. $C_{11}H_{17}Cl$ requires C, 71·5; H, 9·2%) (cf. Sobotka and Chanley [3] give b. p. 96°/14 mm., n_D^{20} 1·5030, analysis C, 72·4; H, 9·7%).

(*b*) 1-Ethynyl-2 : 2 : 6-trimethyl*cyclo*hexanol (16·6 g.) in dry ether (100 ml.) was treated with thionyl chloride (9·0 ml.) and stirred at room temperature for 1 hr. The solvent was distilled off, and the residue heated for 3 hr. on a steam-bath and washed with aqueous sodium hydrogen carbonate. Distillation gave two main fractions, (i) b. p. 86—92°/15 mm., (ii) b. p. 92—94°/15 mm., which were the chloride (II) (5·5 g., 30%) and this mixed with the unchanged alcohol (9·0 g.) respectively, as shown by infrared bands at 3580 s (OH), 3270 s (C=CH), 1950 m (C=C=C), and 730 s cm.$^{-1}$ (C=C=CHCl). A similar experiment in which the product was directly distilled from the reaction mixture without washing the allene (96%) contained only a trace of alcohol (from infrared data) and had b. p. 104—105°/17—20 mm. (Found: C, 70·9; H, 9·4%).

(*c*) 1-Ethynyl-2 : 2 : 6-trimethyl*cyclo*hexanol (16·6 g.) in anhydrous ether (200 ml.) was treated with thionyl chloride (11·9 g.) in ether (200 ml.) and stirred for 2 hr. at room temperature. Working up as in (*b*) and distillation gave one main fraction, b. p. 88—91°/16 mm., identified as the unchanged alcohol by infrared bands at 3580 s (OH) and 3270 s cm.$^{-1}$ (C=CH) and the absence of a band at 1950 cm.$^{-1}$ (C=C=C).

In general, experiments using pyridine gave high analytical figures for carbon and hydrogen owing to the presence of alkenyne, and experiments in the absence of pyridine gave low values owing to traces of addition compound, indicated by infrared bands of varying intensity in the C=C stretching region between 1600 and 1650 cm.$^{-1}$.

The allenic chloride (II) (6·15 g.) and silver nitrate (5·7 g.) in 75% ethanol (70 ml.) were heated under reflux for 2 hr. Silver chloride (4·3 g., 91%) was filtered off and the filtrate neutralised with sodium hydrogen carbonate, evaporated to a small volume, diluted with water, and extracted into ether. Fractionation of the extract gave 1-ethynyl-2 : 2 : 6-trimethyl*cyclo*hexanol (2·8 g.), b. p. 96—98°/18 mm., identified by comparing its infrared spectrum with that of an authentic specimen.

2 : 2 : 6 : 6-*Tetramethyl*cyclo*hexylidenevinyl Chloride*.—1-Ethynyl-2 : 2 : 6 : 6-tetramethyl*cyclo*hexanol (9 g.) in anhydrous ether (50 ml.) gave, by method (*a*), after distillation **2 : 2 : 6 : 6-*tetramethyl*cyclo*hexylidenevinyl chloride*** (8·2 g., 83%), b. p. 82—84°/20 mm. (Found: C, 72·5; H, 9·7; Cl, 18·0. $C_{12}H_{19}Cl$ requires C, 72·5; H, 9·6; Cl, 17·9%), $\nu_{max.}$ 1955 m (C=C=C) and 730 s cm.$^{-1}$ (C=C=CHCl) (no maximum in the ultraviolet region).

[10] (*a*) I. A. Favorskaya, *Zhur. obshchei Khim.*, 1948, **18**, 52; (*b*) T. A. Favorskaya, *J. Gen. Chem.* (*U.S.S.R.*), 1939, **9**, 386; (*c*) T. A. Favorskaya and Zakharova, *ibid.*, 1940, **10**, 446; (*d*) T. A. Favorskaya, *ibid.*, 1942, **12**, 638; (*e*) Nagibina, *Zhur. obshchei Khim.*, 1940, **10**, 427; (*f*) Jacobs and Brill, *J. Amer. Chem. Soc.*, 1953, **75**, 1314.

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2 : 2 : 4 : 4-*Tetramethylpent*-3-*one*.—This was prepared by Whitmore and Stahly.[11] In our variation of the method di*iso*propyl ketone (57 g.) was added in 10 min. to sodamide (23 g.) in anhydrous benzene (200 ml.) at room temperature, then the mixture was heated under reflux (2·5 hr.). Methyl iodide (78 g.) was added dropwise (15 min.) to the cooled mixture, and the whole heated under reflux (15 min.) and set aside overnight. This procedure was repeated twice more, with the same quantities of sodamide and methyl iodide; the mixture was finally altered, dried, and distilled, to give 2 : 2 : 4 : 4-tetramethylpent-3-one (44 g., 62%), b. p. 48—50°/17 mm., n_D^{20} 1·4200 (Found: C, 76·1; H, 12·4. Calc. for $C_9H_{18}O$: C, 76·0; H, 12·6%) (lit.,[11] b. p. 144—150°/740 mm., n_D^{20} 1·4197).

3-tert.-*Butyl*-4 : 4-*dimethylpent*-1-*yn*-3-*ol*.—2 : 2 : 4 : 4-Tetramethylpent-3-one was treated in the usual way with sodium acetylide in liquid ammonia, to give the crude ethynylcarbinol, b. p. 60—72°/12 mm. (21·5 g., 77%), $\nu_{max.}$ 3232 s (C≡CH), 3441 s (OH), and 1685 w cm.$^{-1}$ (CO), indicating that about 30% of ketonic material was present. One repetition of the ethynylation with lithium acetylide in liquid ammonia gave 3-tert.-*butyl*-4 : 4-*dimethylpent*-1-*yn*-3-*ol* (17 g., 61%), b. p. 71—73°/10 mm. (Found: C, 78·5; H, 12·1. $C_{11}H_{20}O$ requires C, 78·6; H, 11·9%) [no infrared band at 1685 cm.$^{-1}$ (CO)].

3-tert.-*Butyl*-1-*chloro*-4 : 4-*dimethylpenta*-1 : 2-*diene*.—*Method* (*a*). The foregoing pentynol (2·8 g.) in anhydrous ether (20 ml.) gave, after fractionation, 3-tert.-*butyl*-1-*chloro*-4 : 4-*dimethylpenta*-1 : 2-*diene* (2·3 g., 74%), b. p. 72—74°/15 mm. (Found: C, 71·0; H, 10·1; Cl, 18·3. $C_{11}H_{19}Cl$ requires C, 70·8; H, 10·2; Cl, 19·0%), $\nu_{max.}$ 1930 m (C=C=C) and 738 s cm.$^{-1}$ (C=C=CHCl) (no ultraviolet maximum).

Method (*b*). This gave the allene (79%), b. p. 98—104°/32 mm., identified by comparison of the infrared spectrum with that of the previous pure sample.

Action of Thionyl Chloride on 1-*Ethynyl*cyclo*hexanol* (12·4 g.).—(*a*) Distillation gave fractions covering a wide range of b. p.s: (i) b. p. 30—60°/15 mm. (3·9 g., 38%), identified, by an infrared band at 3285 s cm.$^{-1}$ (C≡CH) and absence of a band at 3580 cm.$^{-1}$ (OH), as mainly 1-ethynyl-*cyclo*hexene; (ii), b. p. 60—62°/15 mm. (4·2 g.), had infrared bands at 3580 m (OH), 3285 m (C≡CH), 1970 m (C=C=C), and 750 s cm.$^{-1}$ (C=C=CHCl), indicating a mixture of unchanged alcohol and *cyclo*hexylidenevinyl chloride. A substantially pure sample of the allene was prepared by shaking fraction (ii) (3·9 g.) with silver acetate (4 g.) in ethanol (120 ml.) at room temperature for 15 min. The mixture was filtered, diluted with light petroleum, washed, dried, and evaporated, to give the allene chloride, identified by the infrared spectrum which also showed that a small carbonyl impurity had now been introduced (weak band at 1720 cm.$^{-1}$).

Similar results were obtained by using methods (*b*) and (*c*), and additional infrared bands in the C=C stretching region between 1600 and 1650 cm.$^{-1}$ suggested the presence of a rearrangement product.

1-*Chloro*-4-*methyl*-3-iso*propylpenta*-1 : 2-*diene*.—(*a*) 4-Methyl-3-*iso*propylpent-1-yn-3-ol (84 g.) on distillation gave the following fractions: (i) b. p. 45—56°/760 mm., largely ether containing some alkenyne; (ii) b. p. 134—155°/760 mm. (31·5 g.), identified as the alkenyne mixed with about 40% of allene from infrared bands at 3230 s (C≡CH) and 1938 w cm.$^{-1}$ (C=C=C) and the absence of a band at 3510 cm.$^{-1}$ (OH), and an ultraviolet maximum at 225 mμ (ε 6200); (iii) b. p. 155—167°/760 mm. (15·0 g.), identified as the allene mixed with about 20% of enyne from the infrared spectrum. Fractions (ii) and (iii) were combined and refractionated through a 9″ column of Fenske rings to give fractions: (i) b. p. up to 147°/760 mm. (17 g., 23%), identified as 4-*methyl*-3-iso*propylpent*-3-*en*-1-*yne* by the infrared spectrum and ultraviolet absorption [$\lambda_{max.}$ 226 mμ (ε 10,000)]; (ii) b. p. 147—170°/760 mm. (24 g., 25%), which was again fractionated to give material of b. p. 168—170°/760 mm., n_D^{20} 1·4629, identified as 1-*chloro*-4-*methyl*-3-iso*propylpenta*-1 : 2-*diene* (Found: C, 68·4; H, 9·7. $C_9H_{15}Cl$ requires C, 68·1; H, 9·5%) by infrared bands at 1938 m (C=C=C) and 740 s cm.$^{-1}$ (C=C=CHCl) and the absence of ultraviolet light absorption maxima.

(*b*) 4-Methyl-3-*iso*propylpent-1-yn-3-ol (28 g.) gave a product, b. p. 50—52°/10 mm. (24 g.), identified by the infrared spectrum as the allene mixed with about 30% of unchanged alcohol.

(*d*) In this method the alcohol (28 g.) was treated with thionyl chloride in the presence of 2% of pyridine. Distillation gave a product, b. p. 51—57°/11 mm. (27 g.), shown by infrared bands at 1938 m (C=C=C) and 3232 w cm.$^{-1}$ (C≡CH) and no band at 3580 cm.$^{-1}$ (OH) to be a mixture of the allene and enyne.

(*e*) In this method the alcohol (28 g.) and thionyl chloride (24 g.) were added dropwise and

[11] Whitmore and Stanly, *J. Amer. Chem. Soc.*, 1933, **55**, 4155.

XUM

simultaneously to boiling dioxan (100 ml.). When half the liquid had been added a copious evolution of hydrogen chloride began; the product was refluxed for 1 hr. at the end of the addition, by which time evolution of hydrogen chloride had ceased, and then taken up in light petroleum, washed, dried, and distilled to give a main fraction, b. p. 65—66°/17 mm. (23 g.) (72·0%), identified as the allene by infrared bands at 1938 s (C=C=C) and 740 s cm.$^{-1}$ (C=C=CHCl).

1-*Chloro*-3 : 4 : 4-*trimethylpenta*-1 : 2-*diene*.[10b]—(*a*) 3 : 4 : 4-Trimethylpent-1-yn-3-ol (6·3 g.) gave on distillation one main fraction, b. p. 60°/25 mm. (2·5 g., 35%), identified as 1-chloro-3 : 4 : 4-trimethylpenta-1 : 2-diene by bands at 1950 m (C=C=C) and 730 s cm.$^{-1}$ (C=C=CCl), containing about 10% of acetylenic impurities (band at 3300 w cm.$^{-1}$).

(*c*) Unchanged alcohol was obtained.

(*e*) By this method, but with the addition of pyridine (8 g.), when the dioxan became saturated with hydrogen chloride, the alcohol (12·6 g.) gave three fractions on distillation: (i) b. p. 56—60°/16 mm. (1·0 g.), 3-*tert.*-butylbut-3-en-1-yne containing some allene, having $\nu_{max.}$ 3270 m (C≡CH), 1945 w (C=C=C), and 906 s cm.$^{-1}$ (C=CH_2) and no band at 3580 cm.$^{-1}$ (OH); (ii) b. p. 62—63°/15 mm., 1-*chloro*-3 : 4 : 4-*trimethylpenta*-1 : 2-*diene* (6·8 g., 47%), $\nu_{max.}$ 1945 m (C=C=C) and 735 s cm.$^{-1}$ (C=C=CCl) (Found: C, 65·9; H, 8·9. $C_8H_{13}Cl$ requires C, 66·4; H, 9·0%); and (iii) b. p. 63—70°/15 mm. (1·3 g.), allene mixed with some rearrangement product, giving infrared bands between 1600 and 1650 cm.$^{-1}$.

3-iso*Butyl*-1-*chloro*-5-*methylhexa*-1 : 2-*diene*.—(*a*) 3-*iso*Butyl-5-methylhex-1-yn-3-ol (33·6 g.), on distillation, gave two main fractions: (i) b. p. up to 91°/16 mm. (21·5 g.), 3-*iso*butyl-5-methylhex-3-en-1-yne containing about 30% of the allene, $\lambda_{max.}$ 224 mμ (ε 8700), $\nu_{max.}$ 3250 s (C≡CH), 1950 w (C=C=C), and 735 w cm.$^{-1}$ (C=C=CCl) and no peak at 3400 cm.$^{-1}$ (OH); (ii) b. p. 94—100°/20 mm. (3·0 g., 8·0%), 3-iso*butyl*-1-*chloro*-5-*methylhexa*-1 : 2-*diene* (Found: C, 71·0; H, 10·1. $C_{11}H_{19}Cl$ requires C, 70·8; H, 10·2%), $\nu_{max.}$ 1950 m (C=C=C) and 835 s cm.$^{-1}$ (C=C=CCl).

(*b*) Distillation gave fractions, b. p. 59—92°/17 mm., which were identified by infrared and ultraviolet spectra as various mixtures of alkenyne, allene, and unchanged alcohol.

(*d*) These conditions gave similar results to (*b*).

3-*Chloro*-3-*phenylprop*-1-*yne*.—(*a*) 1-Phenylprop-2-yn-1-ol (6·5 g.) in anhydrous ether (20 ml.) afforded on distillation a main fraction, b. p. 76—78°/15 mm. (4·1 g., 54%), identified by an infrared band at 3290 s cm.$^{-1}$ (C≡CH) and the absence of a band at 3580 cm.$^{-1}$ (OH), and the absence of a maximum in the ultraviolet spectrum, as 3-chloro-3-phenylprop-1-yne.

(*b*) By this method 1-phenylprop-2-yn-1-ol (13·2 g.) in anhydrous ether (100 ml.) gave two fractions: (i) b. p. 68°/5 mm. (8·9 g., 59%), $\nu_{max.}$ 3290 s cm.$^{-1}$ (C≡CH), no band at 3580 cm.$^{-1}$ (OH), 3-chloro-3-phenylprop-1-yne; (ii) b. p. 68—70°/5 mm. (1·8 g.), the normal chloride contaminated with cinnamaldehyde as shown by a new infrared band at 1675 w cm.$^{-1}$ (C=C·CHO) and formation of a 2 : 4-dinitrophenylhydrazone (from chloroform–methanol), m. p. 254° (lit., 255°).

(*c*) This method gave the unchanged alcohol, identified by its infrared spectrum.

(*d*) Distillation gave one main fraction, b. p. 64—66°/4 mm. (67%), identified by infrared spectrum as 3-*chloro*-3-*phenylprop*-1-*yne* (Found: C, 71·4; H, 4·8. C_9H_7Cl requires C, 71·8; H, 4·6%).

1-*Chlorohexa*-1 : 2-*diene*.[9]—(*a*) Hex-1-yn-3-ol (19·6 g.) gave the two main fractions: (i) b. p. 65°/20 mm. (6 g.), unchanged alcohol, identified by the infrared spectrum; (ii) b. p. 152—153°/20 mm. (9·5 g., 39%), containing sulphur (about 11·5%), $\nu_{max.}$ 3300 s (C≡CH) and 1206 cm.$^{-1}$ (SO_3) indicating that this material was di-(1-propylpropynyl) sulphite.

(*b*) Hex-1-yn-3-ol (9·8 g.) gave a main fraction, b. p. 38—40°/23 mm., identified by infrared bands at 3170 s (C≡H) and 1939 w cm.$^{-1}$ (C=C=C) and the absence of an ultraviolet maximum as 3-chlorohex-1-yne containing about 10% of 1-chlorohexa-1 : 2-diene.

(*e*) This method gave a similar result to (*b*), but the yield of allene increased to 20%, as estimated from the infrared spectrum.

The authors are indebted to Dr. R. E. Bowman and Miss E. M. Tanner of Parke Davis & Co. Ltd., and Mr. R. F. Branch of the Ministry of Supply for infrared spectra. Some microanalyses were carried out by Imperial College of Science and Technology. We acknowledge a grant from the research fund of the Chemical Society and thank Dr. A. I. Vogel for generous research facilities.

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XUM

7. *Spectrophotometry in the Far-ultraviolet Region. Part II.* Absorption Spectra of Steroids and Triterpenoids.*

By D. W. Turner.

Thirty-six spectra of steroids and triterpenoids in hexane are presented together with those of simpler model compounds. The necessity for introducing a correction for hydrocarbon skeletal absorption when determining $\lambda_{max.}$ of the ethylene band is noted. Exceptions to a correlation of $\lambda_{max.}$ with the number of ethylene substituents are discussed and a relationship is postulated between steric strain and certain features of far-ultraviolet absorption.

Absorption by the ethylene chromophore in the far-ultraviolet region, the result of excitation to two upper states of similar energy ($N \longrightarrow V$ and $N \longrightarrow R$, separately distinguished in only the simplest compounds), is sensitive to replacement of ethylenic hydrogen atoms by alkyl radicals. The resultant bathochromic shift of the broad intense absorption band has been described in terms of a dipole-moment vector effect [1,2] (the result of loss of symmetry of the environs of the ethylenic double bond), or simply as an additive result of progressive substitution.[3] We now describe a series of spectra in which both effects can be discerned and show the effect of steric strain to be of comparable importance.

Attempts to use the alkylation shift diagnostically in the field of steroids and triterpenoids have been limited to measurements of the long-wavelength edge of this band [4,5,6] (above 2050 Å) and if intensity changes here are to be taken as reflecting the changes in the position of the maximum it must be assumed that the shape of the band is not altered. There is no experimental justification for this assumption; indeed relatively small changes in structure can cause marked alterations in appearance of the spectra of simpler compounds,[7] and the present investigation was undertaken partly to examine to what extent " end absorption " truly reflected the position of the maximum and the shape of the whole band.

Results and Discussion

In many of the examples studied (Table 1) the experimental absorption curve corrected for absorption by the solvent (Figs. 1 and 2*C*) showed no maximum and further absorption arising presumably from the complex carbon skeleton must overlie the falling edge of the ethylenic band at shorter wavelengths (none of the functional groupings present except carbonyl gives rise to appreciable absorption in this region). Examination of the spectra of the corresponding saturated materials (Fig. 2*D*) confirmed this; high-intensity absorption is exhibited (ε approaching 10^4) at 1760 Å related to the number of quaternary carbon centres present in the molecule.[8] The ethylenic spectra were corrected for this skeletal absorption either by subtraction of the curve for the exactly corresponding dihydro-compound, or of that of one having essentially the same carbon skeleton, number of quaternary carbon centres, and substituent groups. The resultant corrected curves (broken line) show maxima which, in many cases, resemble in shape and $\lambda_{max.}$ those of simpler olefins [compare

* Part I, *J.*, 1957, 4555.

[1] Gary and Pickett, *J. Chem. Phys.*, 1954, **22**, 599, 1266.
[2] Semenow, Harrison, and Carr, *ibid.*, p. 638.
[3] See, for example, Potts, *ibid.*, 1955, **23**, 73.
[4] Bateman and Koch, *J.*, 1944, 600.
[5] Halsall, *Chem. and Ind.*, 1951, 867.
[6] Bladon, Henbest, and Wood, *J.*, 1952, 2737.
[7] See, for example, Carr and Stücklen, *J. Chem. Phys.*, 1936, **4**, 760.
[8] Turner, *Chem. and Ind.*, 1958, 626.

XUM

TABLE 1.

Spectrum no.	Compound (in hexane unless stated)	Spectrum no.	Compound (in hexane unless stated)
1	*cyclo*Hexene	24	Euph-8-en-3-yl acetate
2	Cholest-2-ene	25	Ergost-8(14)-en-3-ol
3	Pregn-2-en-20-one	26	*iso*Lanost-3-ene
4	Cholest-6-en-3-yl acetate [d]	27	Δ^9-Octalin [b]
5	2-Methylene*cyclo*hexan-1-ol [a]	28	12-Oxo-β-amyran-3-yl acetate
6	2-Methylene*cyclo*pentan-1-ol [a]	29	Moradiol diacetate oxide
7	Lupeol acetate	30	Lupan-3-yl acetate
8	2 : 4 : 4-Trimethylpent-1-ene	31	Coprostigmastan-3-yl acetate
9	Stigmast-22-en-3-yl acetate	32	3-Methoxycholestane
10	Ergost-22-en-3-yl acetate	33	Cholestane
11	Cholesterol	34	5β-Androstane [c]
12	3-Methylcholest-2-ene	35	Noroleana-16 : 18-dien-3β-ol
13	Cholest-5-ene	36	5α-Androstan-3β-yl acetate [c]
14	17-Hydroxy-17-methylandrost-5-en-3-yl acetate	37	5α-Androstane [c]
15	Androst-5-en-17β-yl acetate	38	5α-Androstan-3α-ol [c]
16	Cholest-5-en-3α-ol [a]	39	*iso*Bornyl acetate *
17	Cholest-4-ene	40	2 : 2-Dimethylbutane *
18	3-Hydroxyandrost-9(11)en-17-one	41	*cis*-Pinane
19	Lanost-7-en-3-yl acetate	42	*iso*Bornyl acetate
20	Androst-7-en-3β : 17β-diol diacetate	43	α-Amyrin acetate
21	Lanost-7-en-3-one	44	α-Pinene
22	Cholest-7-en-3-ol	45	Ergost-9(11)-en-3β-yl acetate [d]
23	Lanost-8(9)-en-3-yl acetate	46	β-Ergosten-3-ol [d]
		47	1-Methyl*cyclo*hexene [d]

The author is indebted to the following for the samples indicated: [a] Mr. R. P. Houghton (Chemistry Dept., Imperial College). [b] Dr. L. M. Jackman (Chemistry Dept., Imperial College). [c] Mr. P. M. Jones (Medical Research Council). [d] Professor H. B. Henbest (University of Belfast). [e] Dr. L. C. King (Northwestern University, Illinois). [f] Ciba (Basle). Compounds 4, 16, 20, 34, 36, 37, 38, were obtained through the M.R.C. Steroid reference collection by the courtesy of Dr. W. Klyne.
* In perfluoro*cyclo*hexane.

FIG. 1.

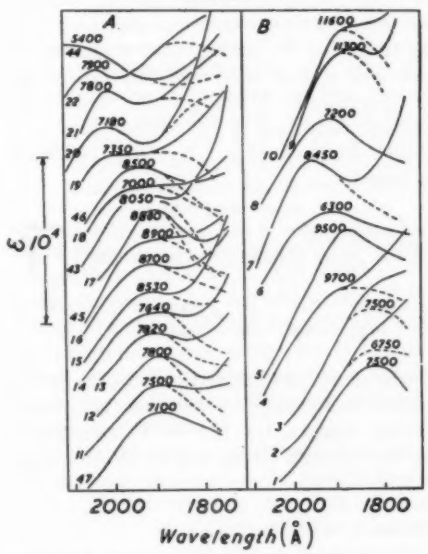
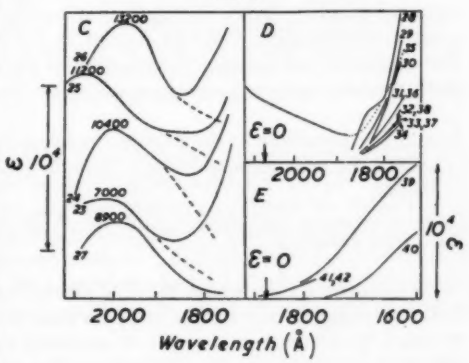


FIG. 2.



Absorption spectra of trisubstituted olefins (A), disubstituted olefins (B), tetrasubstituted olefins (C), and saturated hydrocarbons (D) in hexane, and of some saturated compounds in perfluoromethylcyclohexane (E).

The spectra are at arbitrary intervals on the ε axis, the $\varepsilon_{max.}$ value only being indicated on each curve. All are to the same scale of ε except in *E* where the curves are plotted to half-scale. The arrows on the vertical axis represent 10^4 units of ε.

for example 3-methylcholest-2-ene (12) with 1-methyl*cyclo*hexene (47)]. In such cases a clear correlation exists between $\lambda_{max.}$ and the degree of double-bond substitution:

$\lambda_{max.}$ (Å.)	2000—1960	1930—1880	1880—1820
Number of substituents	4 (Fig. 2*C*)	3 (Fig. 1*A*)	2 (Fig. 1*B*)

Two classes of exception to this grouping can be distinguished: (1) The geminally disubstituted olefins absorb at abnormally long wavelengths (lupeol acetate particularly so, $\lambda_{max.}$ ~1950 Å) attributable to a dipole-moment vector effect; a bathochromic shift of ~100 Å is also observed on comparing the vicinally disubstituted butenes, pentenes, and hexenes with their geminally disubstituted isomers.[1,2] The shift in such cases is not accompanied by increased absorption in the 1700—1800 Å region. (2) By contrast, a bathochromic shift most marked in certain of the trisubstituted group—particularly in Δ^7 compounds—is accompanied by a marked increase of absorption between 1700 Å and 1800 Å. Unusually high end-absorption by ergost-7-ene has been reported, and ascribed to the influence of the neighbouring 8(14) tetrasubstituted position.[6] A similar effect though less marked can be seen in those tetrasubstituted olefins where steric strain may be expected to be present; ergost-8(14)-enol ($\lambda_{max.}$ 2080 Å) in particular shows evidence of additional absorption near 1850 Å. The same association of bathochromic shift with fresh absorption in the far ultraviolet region is shown to the highest degree by α-pinene where considerable strain (entirely in-plane double-bond deformation) is present. It is suggested therefore that spectral abnormalities of the second type are to be ascribed to steric strain and that in the steroids this strain increases in the order Δ^4, Δ^5, $\Delta^{9(11)}$, Δ^{14}, Δ^7 for trisubstituted and $\Delta^{8(9)}$, $\Delta^{8(14)}$ for tetrasubstituted olefins. The corresponding position in the triterpenes shows little spectral abnormality (α-amyrin acetate for example), evidently owing to the replacement by a more flexible six-membered ring of the five-membered ring D, the principal source of rigidity in the steroid molecule.

The difference between spectra of Δ^7- and $\Delta^{9(11)}$-compounds is striking, since it indicates that the magnitude of the strain in the two cases is in the reverse order of that which has been inferred from a study of the C=C stretching frequency.[9] Barton-type models of the various carbon skeletons were constructed and showed a clear difference only in that the terminal ethylene bonds suffered most in-plane distortion in Δ^7-compounds; indeed the spectral abnormality could be related to the angular distortion in the models (Table 2). The magnitude of twisting deformation of the double bond could not, however, be clearly distinguished, and no systematic variation was found.

TABLE 2. *Distortion of the ethylenic terminal-bond angle (referred to* 1-*methyl*cyclo*hexene) in trisubstituted olefinic steroids estimated from Barton-type molecular models.*

Order of increasing bathochromic shift	Δ^2, Δ^3, Δ^4, Δ^5	$\Delta^{9(11)}$	Δ^{14}	Δ^7	α-Pinene
Bond angle distortion	—	+1½°	+3½°	−6°	+6½°

We conclude that whilst the C=C stretching frequency, determined principally by the C=C stretching force constant, may be most sensitive to twisting deformation (not clearly revealed by models) as a result of π-orbital overlap changes, the $N \longrightarrow V$ transition is less so, being more sensitive to in-plane deformation through changes in *sp*-hybridization ratio.

EXPERIMENTAL

The spectrophotometer and technique were described in Part I.

Solvents.—Unless otherwise indicated hexane (Spectrosol) further purified by passage through activated (350° C) silica gel (200 mesh) was used. Perfluoromethyl*cyclo*hexane was purified by repeated extraction with methanol followed by passage through silica gel.

[9] Bladon, *J.*, 1951, 2402.

cyclo*Hexene* (1).—A commercial sample was redistilled from sodium immediately before use, n_D^{20} 1·4460 (lit.,[10] n_D^{22} 1·44507).

α-*Pinene*.—A commercial sample was redistilled before use, and had b. p. 155°/760 mm., n_D^{22} 1·4654.

cis-*Pinane* (41).—α-Pinene in ethanol was hydrogenated at room temperature and pressure with Adams catalyst; hydrogen uptake was quantitative. The product was distilled and a fraction, b. p. 166°/760 mm., n_D^{24} 1·4612, collected (Waterman [11] gives b. p. 166°/755 mm., n_D^{20} 1·4616).

I thank Professor D. H. R. Barton, F.R.S., Dr. P. de Mayo and their associates for analytical samples of many steroids and triterpenoids, and Dr. W. Klyne for making available samples from the Medical Research Council Steroid Reference Collection. Gifts of other samples from Professor H. B. Henbest, Dr. L. M. Jackman, and Mr. R. P. Houghton are also gratefully acknowledged.

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[10] "Dictionary of Organic Compounds," Ed. Heilbron and Bunbury, Eyre and Spottiswoode, London, 1953.
[11] Waterman, *Rec. Trav. chim.*, 1929, **48**, 1191.

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8. *Dissolution of Metals and Alloys. Part I. The Dissolution of Copper in Solutions containing Persulphate Ion.*

By G. C. BOND, B. M. HILL, and R. TENNISON.

The reaction whereby metals dissolve in solutions containing persulphate ion has been examined for its suitability in assessing electronic factors in dissolution processes. Copper readily dissolves in such solutions near room temperature, but the reaction is transport-controlled at $[S_2O_8^{2-}] \leqslant 0{\cdot}025$M and at all concentrations up to 0·1M above 35°. The activation energy for transport control is 5·5 kcal./mole and the order of reaction increases with temperature to a limiting value of 1·2. At $[S_2O_8^{2-}] \geqslant 0{\cdot}25$M the activation energy is constant at 10·3 kcal./mole. Rotation of the copper increases the rate, the more markedly the higher the temperature and the concentration. The rate at 12° and 500 r.p.m. in 0·1M-solutions is substantially free from transport control, and under these conditions the order in persulphate ion is almost zero. The activation energy for the surface process is about 16·5 kcal./mole.

MUCH information has recently been obtained on the effect of the electronic constitution of metals and alloys on their ability to act as heterogeneous catalysts. The necessarily weak chemisorption through which efficient catalysis proceeds is shown by those metals (especially nickel, palladium, and platinum) which have both (i) nearly filled *d*-bands and (ii) a high density of energy levels at the Fermi surface.[1] It is generally assumed that in alloys of one of these metals with a Group IB metal the *d*-band is filled at a concentration of the latter of about 60%, but there is much evidence to show that the nickel–copper system is anomalous.[2]

Relatively little fundamental work has been performed on the effect of electronic constitution on the rate of dissolution of metals and alloys in liquids, although the matter is of great relevance to corrosion. The rate of dissolution of nickel–copper alloys in sea water [3,4] and in sodium chloride solution [5] increases very rapidly with increasing copper content above about 60%. No values for the Arrhenius parameters *A* and *E* were reported.

[1] Dowden, *J.*, 1950, 242.
[2] See, *e.g.*, Coles, *Proc. Phys. Soc.*, 1952, **65**, *B*, 221.
[3] Friend, *J. Inst. Metals*, 1932, **48**, 109.
[4] LaQue, *Amer. Soc. Naval Engrs.*, 1941, **53**, 29.
[5] Uhlig, *Ann. New York Acad. Sci.*, 1954, **58**, 843.

Such systems do not however readily lend themselves to quantitative investigation, and alternative systems have been sought.

It has long been known that many metals dissolve in solutions containing persulphate ions, which act as electron acceptors: the more electropositive metals yield simple cations, *e.g.*, $Cu + S_2O_8^{2-} \longrightarrow Cu^{2+} + 2SO_4^{2-}$. Of the familiar metals, only platinum and gold do not so react.[6] It appeared that this process might be suitable as a means of assessing the electronic influence in dissolutions.

Reactions at solid–liquid interfaces are complicated by transport phenomena.[7] The chief object of this work was to determine under what conditions transport control could be overcome, thus enabling the surface reaction to be studied.

Experimental

Preparation and Estimation of Persulphate Solutions.—Initial experiments were performed with solutions of potassium persulphate, 0·1M-solutions of which were prepared only with difficulty at 18°; they became supersaturated at 0°. Concentrations were estimated by reducing the persulphate with excess of ferrous sulphate and back-titrating the unchanged ferrous ion with 0·1N-potassium permanganate.[8] Potassium persulphate solutions, initially of greater than 99% of the expected concentration, decomposed slowly at room temperature;[9] fresh solutions therefore were prepared daily.

Since it was later desired to carry out experiments with solutions more concentrated than 0·1M, attention was turned to other salts. Evolution of nitrogen was apparent during the attempted preparation of 0·1M-solutions of ammonium persulphate, presumably owing to oxidation of ammonium ion by persulphate ion. Such solutions had initially about 68% of the expected concentration, but thereafter decomposed only slowly: massive decomposition therefore occurs only during the dissolution, perhaps owing to the need to have solid present to nucleate the nitrogen bubbles. Ammonium persulphate solutions were clearly not acceptable for quantitative work.

The ratio of the estimated to the expected concentrations of sodium persulphate solutions is a minimum for solutions expected to be 0·25M (Table 1): no reason for the apparent dependence of this ratio on expected strength can be given. A graph was drawn, and the actual concentration of any solution was calculated by multiplying that expected by a factor obtained by interpolation within the graph. Sodium persulphate solutions decomposed only slowly on standing, but fresh solutions were prepared daily. All solutions were made up at the temperature at which they were to be used.

Table 1. *Expected and estimated concentrations of sodium persulphate solutions.*

Expected (M)	0·1	0·25	0·5	1·0
Estimated (M)	0·0932, 0·0930	0·2290, 0·2285	0·4645	0·940
Estimated/expected	0·932, 0·930	0·916, 0·914	0·929	0·940

Preparation of Copper Specimens.—Copper specimens (*ca.* 1·0 × 1·5 cm.) were cut from a sheet of "AnalaR" copper foil, 0·11 mm. thick. The removal of superficial tarnish and grease with a commercial metal polish, followed by polishing and washing with acetone, did not lead to reproducible rates. A variety of subsequent treatments was tried: treatment with concentrated hydrochloric acid led to faster but still irreproducible rates, and the finally adopted procedure was to etch the specimen for 20 sec. in 8M-nitric acid at 18° ± 2°. A standard specimen weighed 0·147 g. before and close to 0·140 g. after etching: the geometic area of the specimen after etching was estimated to be 3·05 cm.^{2}.

Procedure.—The reaction was followed by periodically determining the loss in weight of the copper. For experiments performed without rotation of the copper, 50 ml. of the solution were placed in a 100 ml. conical flask and brought to the required temperature: the copper was

[6] Mellor, "Comprehensive Treatise on Inorganic and Theoretical Chemistry," Longmans, London, 1930, Vol. X, p. 468.
[7] See, *e.g.*, Bircumshaw and Riddiford, *Quart. Reviews*, 1952, **6**, 157.
[8] Scott and Furman, "Standard Methods of Chemical Analysis," Technical Press Ltd. London, 1952, 5th edn., Vol. I, p. 922.
[9] Bawn and Margerison, *Trans. Faraday Soc.*, 1955, **51**, 925.

placed in a holder constructed from thin glass rod (Fig. 1*a*) and then inserted into the solution. The copper was removed, washed, dried and weighed at intervals of 5, 10, or 15 min.

In some experiments the copper was rotated in 75 ml. of the solution in a 100 ml. conical flask, a holder of the type shown in Fig. 1*b* being used. The holder was rotated by an electric motor whose speed was manually adjusted with a rheostat; rates of revolution were measured by a tachometer. Other procedures were as before.

Standard methods of temperature control and measurement were employed.

FIG. 1. (*a*) *Holder used when there was no rotation of the copper.* (*b*) *Holder used when the copper was rotated.*

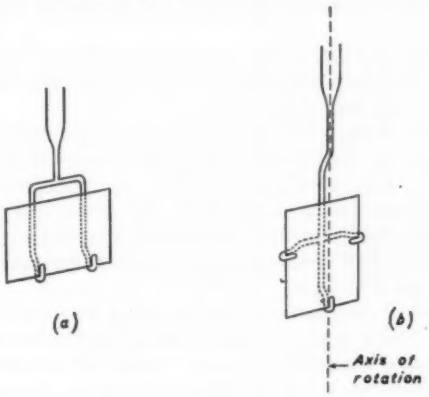
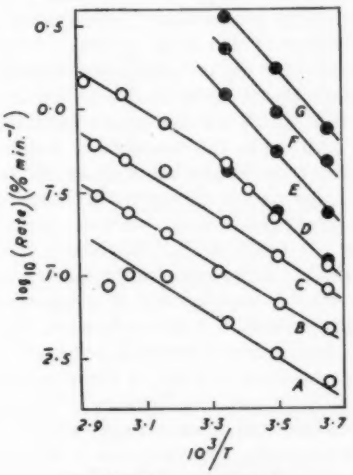


FIG. 2. *Dependence of* $\log_{10}$ *rate on reciprocal absolute temperature at various concentrations of persulphate ion.*



○ Potassium persulphate.
● Sodium persulphate.

A, 0·0125M; *B*, 0·025M; *C*, 0·050M; *D*, 0·10M; *E*, 0·25M; *F*, 0·50M; *G*, 1·00M.

Results and Discussion

Expression of Rates and Shapes of Weight Loss–Time Curves.—The geometric area of a specimen is to a close approximation proportional to its weight for small deviations from standard size. The rate being assumed to be proportional to the area, such deviations were allowed for by expressing rates in terms of a percentage loss in weight, $(\Delta w/w_0) \times 100$, where w_0 is the initial weight (after etching) and Δw the change in weight in the same units. Thus a rate of 1·0% min.$^{-1}$ corresponds to the dissolution of 1·47 mg. of copper min.$^{-1}$ from a standard specimen, and therefore to 0·48 mg. of copper cm.$^{-2}$ min.$^{-1}$. This is equivalent to a rate of change in persulphate-ion concentration of $2{\cdot}62 \times 10^{-7}$ g.-ion l.$^{-1}$ min.$^{-1}$ cm.$^{-2}$. After 50% dissolution, the geometric area was decreased only by about 1% and no change in rate was noticed until more than 80% of the copper had dissolved, provided that the initial concentration of persulphate ion was sufficiently high. When this condition was not fulfilled ($[S_2O_8^{2-}] < 0{\cdot}025$M), rates decreased from the start and were proportional to the instantaneous concentration of persulphate ion. First-order rate constants were then determined and the initial rates calculated therefrom.

Dependence of Rates on Temperature and on Persulphate-ion Concentration with Potassium Persulphate and No Rotation of the Copper.—The results are shown in Fig. 2. The activation energies shown at the two lowest concentrations are constant over the whole range of temper-

ature at 5·5 kcal./mole. At the two higher concentrations, the activation energies also have this value above about 35°, but between 0° and 35° the value for 0·05M-solutions is 6·5 and for 0·10M-solutions 9·1 kcal./mole. These and subsequently quoted activation energies are not uncertain by more than ±0·2 kcal./mole.

Now the activation energy of a process whose rate is determined by transport of ions through a solution will be approximately that for the diffusion of ions through the solution, typically about 1 kcal./mole greater than E_ν, the activation energy for kinematic viscous flow.[10] E_ν for water has been estimated as 4·40 ± 0·05 kcal./mole between 0° and 25° (Orr and Butler [11] give 4·2 kcal./mole between 0° and 45°), and for 0·1M-potassium persulphate solution as 4·1 kcal./mole in the same temperature range. The lower value in the latter case arises because the solution becomes progressively *less* viscous than water with decreasing temperature, presumably owing to the progressively increasing degree of hydration of the ions, which "de-polymerises" the water structure. The kinematic viscosity for the potassium persulphate solution is 1·480 centistokes at 5° as against 1·519 centistokes for water at this temperature.

It is concluded that under conditions where the activation energy of the dissolution is 5·5 kcal./mole the reaction is completely transport-controlled, and that for solutions greater than 0·025M below about 35° transport control in not complete.

These results also give the following values of the order of the reaction in persulphate-ion concentration at various temperatures in 0·0125—0·1M-potassium persulphate: 0·75 (0°), 0·92 (12·0°), 1·02 (25·0°), 1·10 (42·7°), 1·20 (55·0°), 1·19 (65·0°). A temperature-dependent order necessarily follows from a concentration-dependent activation energy: the order is independent of temperature when the reaction is transport-controlled at all concentrations, but no explanation can be offered for a limiting value greater than unity. The significance of reaction order will be reverted to later.

Dependence of Rates on Temperature and on Persulphate-ion Concentration with Sodium Persulphate and No Rotation of the Copper.—The above results show a concentration-dependent activation energy, and to determine whether a limiting value was attained with increasing concentration it was necessary to use a more soluble persulphate, namely, sodium persulphate. Results are shown in Fig. 2. Rates obtained by use of either the sodium or the potassium salt (0·1M) are closely similar at all temperatures: the activation energies are therefore also similar (8·8 as against 9·1 kcal./mole). At all concentrations higher than 0·1M the activation energy is constant at 10·3 kcal./mole, and this limiting value implies no change in the degree of transport control with increasing concentration greater than 0·1M. Whether transport control is completely absent under these conditions has yet to be established.

The dependence of order of reaction on temperature for 0·1—1·0M-sodium persulphate solutions is 0·78 (0°), 0·87 (12·0°), 1·06 (25·0°; 0·1—0·5M only). The values at each temperature correspond closely with those for potassium persulphate solutions. The full results for the dependence of the rate on concentration at 25° are shown in Fig. 3: the order is 1·06 for concentrations less than about 0·5M, whereafter there is a progressive decrease in order with increasing concentration. Now the degree of transport control varies with concentration below about 35°: apparent reaction orders less than unity are obtained where partial transport control operates, and they decrease with decreasing temperature, *viz.*, as the degree of transport control at constant concentration decreases. Orders at all temperatures should be unity at sufficiently low concentrations, and the implication is that zero orders would obtain at sufficiently high concentrations. The results in Fig. 3 show this trend clearly. The reaction might well be of zero order when there is no transport control if persulphate ions are adsorbed at the copper surface before reacting; a limiting rate would obtain when the persulphate-ion concentration in solution is high enough to form a monolayer of ions at the copper surface.

[10] Riddiford, *J. Phys. Chem.*, 1952, **56**, 745.
[11] Orr and Butler, *J.*, 1935 1273.

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Dependence of Rate on Temperature and on Persulphate-ion Concentration at Various Rates of Rotation of the Copper in Potassium Persulphate Solutions.—The critical test for the absence of transport control in reactions at solid–liquid interfaces is the independence

FIG. 3. *Dependence of* log *rate on* log $[S_2O_8^{2-}]$ *at 25° with sodium persulphate concentration.*

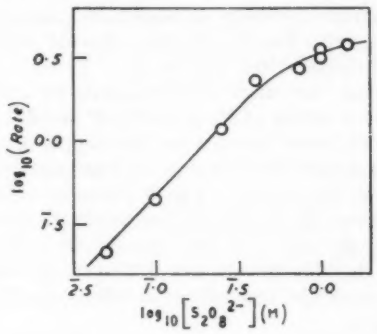
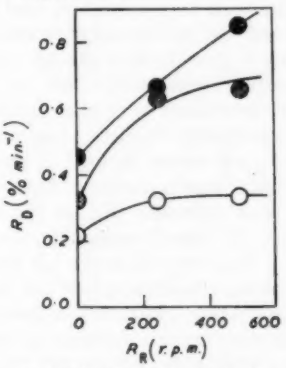


FIG. 4. *Dependence of rate* R_D *on rate of rotation* R_R *for* 0·1M*-potassium persulphate at various temperatures.*



○ 12·0°; ● 19·0°; ● 25·0°

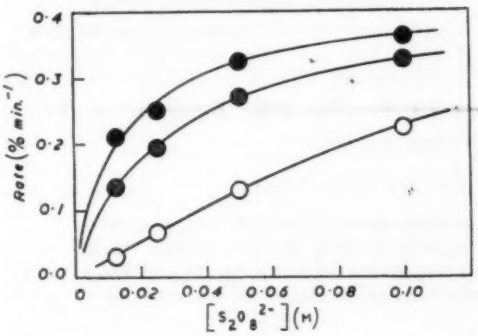
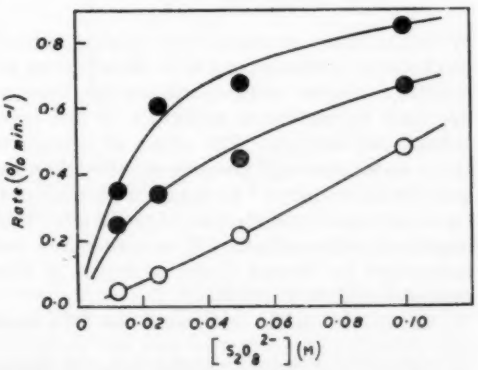


FIG. 5. *Dependence of rate on concentration at 12·0° with various rates of rotation.*

○ No rotation; ● 250 r.p.m.; ● 500 r.p.m.

FIG. 6. *Dependence of rate on concentration at 25·0° with various rates of rotation.*

○ No rotation; ● 250 r.p.m.; ● 500 r.p.m.



of the reaction rate, R_D, of the rate of rotation of the solid, R_R (see Fig. 4). At 12° R_D becomes independent of R_R at rates greater than about 350 r.p.m.: R_D at 500 r.p.m. is 0·335% min.$^{-1}$, or $1·94 \times 10^{-7}$ g.-ion of $S_2O_8^{2-}$ min.$^{-1}$ l.$^{-1}$ cm.$^{-2}$, and this is the rate of

dissolution at this temperature uninhibited by transport phenomena. Fig. 4 shows as expected that progressively higher values of R_R are required to overcome transport control as the temperature is raised, and while R_D at 19° and 500 r.p.m. (0·660% min.$^{-1}$) may be substantially free from such control, R_D is almost proportional to R_R at 25°. As it proved impossible to rotate the copper at speeds much in excess of 500 r.p.m., since turbulent flow sets in between 700 and 800 r.p.m. and eddies then form around it, there is only a small temperature range (15—20°) in which the activation energy of the true dissolution process can be determined, and little accuracy can therefore be expected. The rates at 12° and 19° at 500 r.p.m. correspond to an activation energy of about 16·5 kcal./mole, which is considerably greater than the limiting value found with concentrated solutions of sodium persulphate when the copper was not rotated (10·3 kcal./mole).

Experiments were also performed to determine the effect of persulphate-ion concentration (0·0125—0·1M) on reaction rates at various values of R_R at both 12° and 25°; the results are shown in Figs. 5 and 6 together with those found when the copper was not rotated. Fig. 5 confirms that the order in persulphate ion is low when transport control has been overcome (*i.e.*, in the region of 0·1M at 500 r.p.m.). Fig. 6 shows as expected that at 25° higher concentrations for a given value of R_R are required to attain the limiting rate. Experiments involving rotation of the copper have not been carried out in sodium persulphate solutions, but the results indicate that the use of, say, 1·0M-persulphate-ion concentration and an R_R of 500 r.p.m. would enable the true rate of the dissolution to be determined over a substantial temperature range.

We are grateful to Dr. John Shorter who first drew our attention to this reaction.

THE UNIVERSITY, HULL. [*Received, August 8th*, 1958.]

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9. *Oxygen Heterocycles. Part IX.* The Elbs Reaction in the Dibenzofuran Series.*

By NG. PH. BUU-HOÏ and DENISE LAVIT.

The Elbs reaction of 2-*o*-toluoyldibenzofuran is shown to give a mixture of naphtho(2′ : 3′-1 : 2)- and naphtho(2′ : 3′-2 : 3)-dibenzofuran. 2-(2-Methyl-1-naphthoyl)dibenzofuran undergoes the same reaction, to give also a mixture of the two possible phenanthrodibenzofurans, whose properties have been investigated.

WHEREAS many nitrogen- and sulphur-containing heterocyclic analogues of condensed carcinogenic hydrocarbons have already been tested for tumour- and/or growth-inhibitory activity,[1] similar oxygen-heterocycles have rarely been investigated. A convenient approach to condensed molecules of this type was Elbs pyrolysis of suitable oxygen-heterocyclic ketones. The choice of ketones with favourable structures was limited to those whose carbonyl group is not directly attached to the furan ring, in view of Badger and Christie's failure [2] to obtain a phenanthrofuran from 2 : 5-dimethyl-3-(2-naphthoyl)-furan because of resinification of the latter. Pyrolysis of 2-*o*-toluoyl- (I) and 2-(2-methyl-1-naphthoyl)-dibenzofuran (II) was therefore investigated. These ketones were obtained isomer-free by Friedel–Crafts acylation of dibenzofuran with *o*-toluoyl chloride and 2-methyl-1-naphthoyl chloride.[3]

Ketone (I) readily underwent the Elbs reaction, to give a mixture of two crystalline

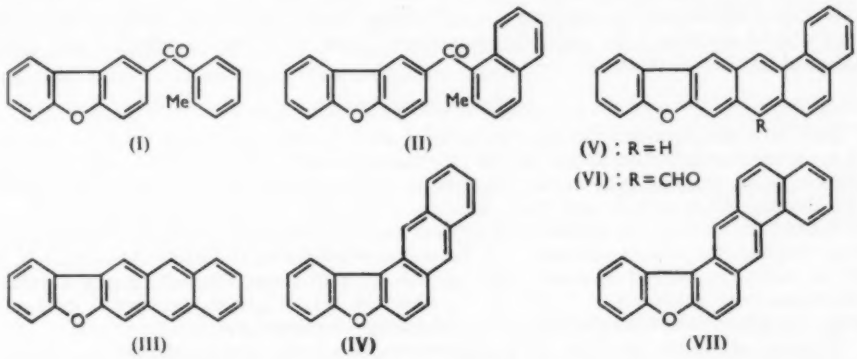
* Part VIII, Buu-Hoï, Saint-Ruf, Loc, and Xuong, *J.*, 1957, 2593.

[1] Cf. Lacassagne, Buu-Hoï, Daudel, and Zajdela, "Advances in Cancer Research," Academic Press, New York, 1956, Vol. IV.

[2] Badger and Christie, *J.*, 1956, 3435.

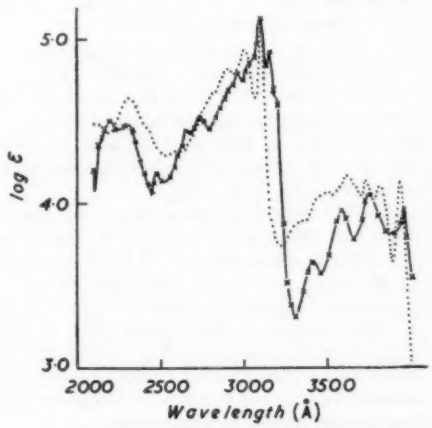
[3] Cf. Galewsky, *Annalen*, 1891, **264**, 189; Borsche and Bothe, *Ber.*, 1908, **41**, 1843; Mosettig and Robinson, *J. Amer. Chem. Soc.*, 1935, **57**, 2186; Buu-Hoï and Royer, *Rec. Trav. chim.*, 1948, **67**, 175.

products, one of which was assigned the linear structure of naphtho(2′ : 3′-2 : 3)dibenzofuran (III) on account of its high m. p. (322°) and pronounced yellow colour; the isomeric naphtho(2′ : 3′-1 : 2)dibenzofuran (IV), which, because of its greater solubility in hydrocarbons, could easily be separated from (III), had a considerably lower m. p. (173°) and was only pale yellow. The yield of the linear compound was appreciably the lower, which



shows that the known tendency of Elbs reactions to favour the angular structures [4] also applies to oxygen-heterocyclic molecules.

The pyrolysis of ketone (II) unexpectedly gave only a low yield, of two isomeric yellow compounds. Although there was less marked difference in colour than between compounds (III) and (IV), ultraviolet absorption measurements (see Figure) suggested that the



· · · *Compound* (VII). —— *Compound* (V).

more absorbing isomer (m. p. 247°) was phenanthro(3′ : 2′-2 : 3)dibenzofuran (V), the other compound then being phenanthro(2′ : 3′-1 : 2)dibenzofuran (VII). Chemical support for these assignments lay in the differing behaviour of the two isomers on formylation with *N*-methylformanilide in presence of phosphorus oxychloride. Compound (V), which possesses a reactive *meso*-position, gave an aldehyde (VI), whilst the isomer (VII), whose *meso*-anthracenic positions are both sterically hindered, failed to react. This accords with

[4] Cf. Cook, *J.*, 1931, 487; 1932, 1472.

the fact that of the two *meso*-anthracene positions in benz[*a*]anthracene only the sterically unencumbered position 7 can be formylated.[5]

If the Elbs reaction of 2-(2-methyl-1-naphthoyl)dibenzofuran was for only a short time, a third product was isolated, which was richer in oxygen than compounds (V) and (VII) and was probably an anthrone-like derivative.

The two phenanthrodibenzofurans (V) and (VII) can be considered as benz[*a*]-anthracenes substituted in positions 8 and 9 (Ring Index numbering), both of which are known to be significant for carcinogenic activity,[6] and these two compounds are under biological test in this Institute.

Experimental

2-o-*Toluoyldibenzofuran* (I).—To a solution of dibenzofuran (10 g.) and *o*-toluoyl chloride (18 g.) in anhydrous carbon disulphide (75 c.c.), finely powdered aluminium chloride (9 g.) was added in small portions with stirring, and the mixture left for 3 days at room temperature. After decomposition with ice and hydrochloric acid, the product was taken up in chloroform, the chloroform solution was washed with 5% aqueous sodium hydroxide, then with water, and dried (Na_2SO_4), the solvent removed, and the residue fractionated *in vacuo*. The *ketone*, b. p. 267°/12 mm., crystallised as prisms (13·5 g.), m. p. 100° (from ethanol), giving a yellow halochromy with sulphuric acid (Found: C, 83·8; H, 5·1. $C_{20}H_{14}O_2$ requires C, 83·9; H, 4·9%). Acidification of the alkaline liquors yielded 8 g. of *o*-toluic acid.

Pyrolysis of Ketone (I).—The foregoing ketone (13 g.) was gently refluxed for 1 hr. at atmospheric pressure, with removal of water, and the product was then distilled *in vacuo*, yielding an orange-yellow resin (10 g.), which was taken up in boiling toluene (400 c.c.). The yellow precipitate formed on cooling recrystallised from toluene, giving *naphtho*(2′ : 3′-2 : 3)-*dibenzofuran* (III), yellow leaflets (1·8 g.), m. p. 322°, the halochromy with sulphuric acid being orange, rapidly becoming brown (Found: C, 89·2; H, 4·5. $C_{20}H_{12}O$ requires C, 89·5; H, 4·5%). The toluene mother-liquors yielded, after concentration, a pale yellow precipitate (4·2 g.) which, on repeated crystallisation from *cyclo*hexane, furnished *naphtho*(2′ : 3′-1 : 2)*dibenzofuran* (IV), pale yellow needles (3 g.), m. p. 173°, with halochromy in sulphuric acid the same as for the isomer (Found: C, 89·4; H, 4·6%).

2-(2-*Methyl*-1-*naphthoyl*)*dibenzofuran* (II).—2-Methyl-1-naphthoic acid was prepared by carboxylation of 2-methyl-1-naphthylmagnesium bromide. To a solution of 2-methyl-1-naphthoyl chloride (54 g.) and dibenzofuran (20 g.) in dry carbon disulphide (150 c.c.), aluminium chloride (17·5 g.) was added portionwise, and the mixture left for 3 days, then worked up as for compound (I). The portion boiling at 260—270°/0·5 mm. crystallised as prisms (20·5 g.), m. p. 160°, from ethanol, and gave an orange-yellow halochromy with sulphuric acid (Found: C, 85·5; H, 5·0. $C_{24}H_{16}O_2$ requires C, 85·7; H, 4·8%).

Pyrolysis of Ketone (II).—(*a*) The foregoing ketone (10 g.) was gently refluxed for 1 hr.; the product was distilled *in vacuo*, and taken up in benzene, giving a less-soluble portion which crystallised from benzene to furnish *phenanthro*(3′ : 2′-2 : 3)*dibenzofuran* (V), bright yellow leaflets (0·6 g.), m. p. 247°, giving no colour in cold sulphuric acid but on heating a blue halochromy which rapidly changed to greenish-brown (Found: C, 90·2; H, 4·4. $C_{24}H_{14}O$ requires C, 90·5; H, 4·4%). The benzene mother-liquors gave, on concentration, *phenanthro*-(2′ : 3′-1 : 2)*dibenzofuran* (VII), colourless needles (0·3 g.), m. p. 227° (from ethanol–benzene), giving with hot sulphuric acid a reddish halochromy rapidly becoming greenish-brown (Found: C, 90·2; H, 4·4%). This compound gave from benzene an orange-red picrate, which decomposed on recrystallisation from ethanol or when heated above 150°.

(*b*) Pyrolysis of the ketone (II) (10 g.), when effected in 20 min., yielded, in addition to compounds (V) (0·2 g.) and (VII) (0·1 g.), a *substance*, crystallising as pale yellow needles (0·5 g.), m. p. 241° (decomp. >230°) (from benzene), giving a deep yellow halochromy with sulphuric acid (Found: C, 85·7; H, 4·7. $C_{24}H_{16}O_2$ requires C, 85·7; H, 4·8%). This compound, for which the analytical results suggest the structure of a dihydroanthrone, was not detected in the first pyrolysis experiment.

Formylation of Phenanthro(3′ : 2′-2 : 3)*dibenzofuran* (V).—A mixture of compound (V) (0·57 g.), *N*-methylformanilide (0·36 g.), phosphorus oxychloride (0·38 g.), and dry *o*-dichlorobenzene

[5] Fieser and Hartwell, *J. Amer. Chem. Soc.*, 1938, **60**, 2555.
[6] Cook, *J.*, 1931, 499, 2529.

(10 c.c.) was heated for 7 hr. on a boiling-water bath. After cooling and filtration, the filtrate was treated with saturated aqueous sodium acetate (10 c.c.), and the solvent and *N*-methylaniline were removed by steam-distillation. The yellow solid residue was filtered off, washed with water, dried, and recrystallised several times from benzene to give, along with unchanged material, a small quantity of 1′-*formylphenanthro*(3′ : 2′-2 : 3)*dibenzofuran* (VI), yellow needles (12 mg.), m. p. 255° (Found: C, 86·4; H, 4·1. $C_{25}H_{14}O_2$ requires C, 86·7; H, 4·1%), giving a deep violet halochromy with sulphuric acid. The same formylation, attempted with phenanthro(2′ : 3′-1 : 2)dibenzofuran (VII), resulted only in recovered material, m. p. 227°. The sluggish reactivity of compound (V) and the complete inertia of compound (VII) towards formylation are characteristic of condensed dibenzofurans.[7]

This investigation was supported in part by a research grant from the National Cancer Institute of the National Institutes of Health, U.S. Public Health Service. The authors thank the authorities concerned, and also Miss A. Cheutin for the ultraviolet absorption spectra.

THE RADIUM INSTITUTE, THE UNIVERSITY OF PARIS. [*Received, August 11th*, 1958.]

[7] Buu-Hoï, "Colloque international sur les Hétérocycles oxygénés, Lyon, 1955," Centre National de la Recherche Scientifique, Paris, 1957, p. 111.

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10. *Anionotropic Systems. Part VII.* Reversible Rearrangements of the 1-Naphthyl-3-phenylallyl Alcohols. A Kinetic Determination of the Conjugation Energies of the α- and β-Vinylnaphthalene Systems.*

By (the late) E. A. BRAUDE and P. H. GORE.

The two pairs of 1 : 3-diarylallyl alcohols (I) and (II) where X = α- and β-naphthyl have been synthesised and their reversible, acid-catalysed interconversion has been studied spectrokinetically by a microtechnique. The

(I) HO·CHX·CH=CHPh ⇌ CHX=CH·CHPh·OH (II)

rearrangement of the α-naphthyl derivatives is slightly slower than that of the β-naphthyl derivatives and has slightly higher energies and entropies of activation.

The equilibria lie on the side of the vinylnaphthalene derivatives (II), in the sequence X = α-naphthyl > β-naphthyl > phenyl. The free energies of rearrangement, which are a measure of the resonance energies of the α- and β-vinylnaphthalene relative to the styrene system, are 205 and 35 cal./mole respectively. These values may be compared with those of 760 and 120 cal./mole derived from Coulson and Longuet-Higgins's molecular-orbital calculations. It is apparent that an ethylenic bond conjugates more strongly with a naphthyl than with a phenyl group, but that the observed conjugation energies are rather smaller than those predicted. Possible reasons for this are discussed and it is suggested that steric effects may be a contributory factor in accounting for the relatively low reactivity and conjugation stabilisation of the α-naphthyl derivatives.

IN a previous paper,[1] it was shown that the reversible rearrangement of 1 : 3-disubstituted allyl alcohols HO·CHX·CH=CHY ⇌ CHX=CH·CHY·OH provides an excellent basis for a quantitative comparison of the conjugating properties of X and Y. By using Y = Ph as a standard of reference and varying X, the electronic effects of X relative to phenyl can be assessed from the rates of the forward and the reverse reaction, while from the equilibrium constants the conjugation energy of the system X·CH=CH relative to the styryl system Ph·CH=CH can be determined since the difference will be equal, as a close approximation, to the free energy of the isomerisation. Thus, it was shown [1] that the conjugation energy

* Part VI, *J.*, 1958, 2404.

[1] Part I, Braude and Waight, *J.*, 1953, 419.

(arising from interaction of the π-electrons of an aryl group with those of CH=CH, in the ground state) of the *p*-nitrostyryl system exceeds that of the styryl system by 120 ± 2 cal./mole. This example illustrated two advantages of such a kinetic method of determining resonance energies: the method can be used to increase quite small interactions which could not be accurately deduced from heats of combustion, and it can be employed with systems where alternative thermochemical methods (*e.g.*, heats of hydrogenation) are not readily applicable.

The kinetic approach is particularly suited to the study of condensed aromatic systems and the present work deals with the α- and β-naphthyl derivatives. Several recent rate comparisons are already available, including one based on the irreversible rearrangement [2] of the methyl-naphthylallyl alcohols (X = $C_{10}H_7$, Y = Me), but no previous attempt has been made to determine the conjugation energies of the naphthylvinyl system experimentally, though precise values of these quantities have been predicted from molecular-orbital calculations.

Syntheses.—The 1-naphthyl-3-phenylallyl alcohols were synthesised by standard methods. The alcohol (III) was obtained directly from cinnamaldehyde and α-naphthylmagnesium bromide in 75% yield. This method fails with β-naphthylmagnesium bromide although normal reactions of this Grignard reagent with other carbonyl compounds have been reported.[3,4] The alcohol (V) was therefore synthesised by another route from β-acetylnaphthalene. Condensation with benzaldehyde under acidic or basic conditions gave the same β-naphthyl styryl ketone (VII) (evidently the *trans*-isomer) which was converted into the alcohol (V) by reduction with lithium aluminium hydride at −20°; β-naphthyl phenethyl ketone, formed by 1 : 4-reduction [5] or by prototropic rearrangement [6] of the alcohol, is obtained as a side-product.

(III) α-$C_{10}H_7$·CH(OH)·CH:CHPh
(V) β-$C_{10}H_7$·CH(OH)·CH:CHPh
(VII) $C_{10}H_7$·CO·CH:CHPh

α-$C_{10}H_7$·CH:CH·CHPh·OH (IV)
β-$C_{10}H_7$·CH:CH·CHPh·OH (VI)
$C_{10}H_7$·CH:CH·COPh (VIII)

The isomers (IV) and (VI) were synthesised from the naphthaldehydes. β-Naphthaldehyde was conveniently prepared from 2-naphthonitrile by controlled reduction with lithium aluminium hydride at 0°, after an experiment with benzonitrile had afforded benzaldehyde in good yield. This method has been previously employed for preparing few aliphatic examples [7] but has not been widely used; it appears to work well generally for aromatic derivatives. Since condensation of the naphthaldehydes with acetaldehyde to give the α-naphthylacraldehydes presents difficulties,[3] the aldehydes were converted instead into the 2-naphthylvinyl phenyl ketones (VIII) by reaction with acetophenone: again the same (*trans*-)isomer was obtained under acidic or basic conditions. Reduction of the α-naphthyl derivative (VIII) with lithium aluminium hydride at 0° and −20° gave, not the alcohol (IV), but mainly 3-α-naphthyl-1-phenylpropan-1-ol and 2-α-naphthylethyl phenyl ketone, respectively; at −30°, however, a product estimated spectroscopically to contain not less than 75% of the alcohol (IV) was obtained. Reduction of the β-naphthyl derivative (VIII) at −20° gave the alcohol (VI) in good yield.

Kinetic Measurements.—The two pairs of alcohols (III ⇌ IV) and (V ⇌ VI) are rapidly interconverted in the presence of dilute mineral acid and the reactions were studied

[2] Braude and Fawcett, *J.*, 1950, 800.
[3] Braude, Fawcett, and Newman, *J.*, 1950, 793.
[4] See Kharash and Reinmuth, "Grignard Reactions of Non-metallic Substances," Constable and Co., London, 1954, for other examples.
[5] Cf. Gaylord, "Reduction with Complex Metal Hydrides," Interscience Publishers, New York, 1956, for references to other examples.
[6] Tiffeneau, *Bull. Soc. chim. France*, 1907, **1**, 1209; Nomura, *ibid.*, 1925, **37**, 1245; Burton and Ingold, *J.*, 1928, 904.
[7] Henne, Pelley, and Alm, *J. Amer. Chem. Soc.*, 1950, **72**, 3370; Vandick and Larsen, *ibid.*, 1951, **73**, 3534; Smith and Rogier, *ibid.*, p. 4048; cf. Braude and Wheeler, *J.*, 1955, 320; Soffer and Katz, *J. Amer. Chem. Soc.*, 1956, **78**, 1705.

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under the standard conditions (0·01M-hydrogen chloride in 60% aqueous dioxan) used previously.[2] Although the differences in ultraviolet light absorption between the isomers are smaller than for the aryl-methylallyl alcohols,[3] owing to superposition of absorption due to the aryl and the arylvinyl chromophore, the rearrangements could be followed quantitatively by the spectrokinetic technique. By using a specially designed cell-holder in a thermostat, the reactions could be carried out directly in the absorption cell. In this way, high accuracy was attained on a micro-scale, only a few milligrams of each alcohol being required for investigation at five temperatures. The overall rate constants, determined separately for both members of each pair, were in excellent agreement; thus, for the rearrangement (V ⇌ VI) at 30°, the values 0·243 ± 0·029 and 0·249 ± 0·019 min.$^{-1}$ were obtained from measurements at 2490 Å, and the values 0·249 ± 0·009 and 0·263 ± 0·004 min.$^{-1}$ from measurements at 3000 Å. The absorption curves of the equilibrium

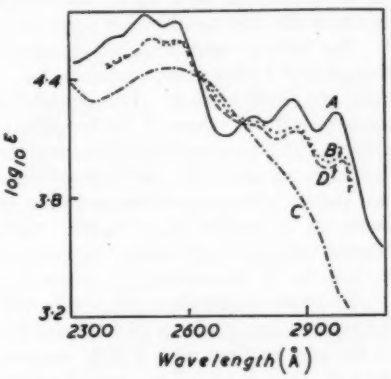


FIG. 1.
A (—), *3-β-Naphthyl-1-phenylallyl alcohol* (VI).
B (. . . .), *Rearranged* (VI).
C (— · — · —), *1-β-Naphthyl-3-phenylallyl alcohol* (V).
D (– – – –), *Rearranged* (V).

mixture obtained from either isomer were identical within experimental error (see Fig. 1) and the equilibrium constants calculated from the extinction coefficients at different wavelengths coincided closely.

RESULTS AND DISCUSSION

The results are collected in Tables 1 and 2. The rates of rearrangement are slightly greater, and the energy of activation is slightly lower, for the β- than for the α-derivative.

TABLE 1. *First-order rate-constants* (*k in min.*$^{-1}$) *for the rearrangements in dioxan–water* (6 : 4) *containing* 0·01M-*hydrogen chloride.*

X·CH(OH)·CH=CHPh ⇌ X·CH=CH·CHPh·OH (k_1, k_{-1})

	X = α-Naphthyl			X = β-Naphthyl		
Temp.	k	k_1	k_{-1}	k	k_1	k_{-1}
30°	0·177	0·103	0·074	0·257	0·132	0·125
35	0·307	0·180	0·127	0·445	0·228	0·217
40	0·540	0·316	0·224	0·749	0·385	0·364
45	0·938	0·549	0·389	1·300	0·668	0·532
50	1·580	0·923	0·657	2·170	1·120	1·050

TABLE 2. *Equilibrium constants* (*K*), *free energies, and activation parameters* (*at* 30°) *for the rearrangements.*

X·CH(OH)·CH=CHPh ⇌ X·CH=CH·CHPh·OH (*K*)

	K	$-\Delta G$ (cal./mole)	ΔE_A (cal./mole)	$\Delta S^\ddagger$ (e.u.)
α-$C_{10}H_7$	1·41	205	21,400	+3
β-$C_{10}H_7$	1·06	35	20,800	0

This is the reverse of the usual sequence of reactivity, but the differences are too small to be of much significance. Of the 3-methyl-1-naphthylallyl alcohols,[2] the β-derivative rearranged more slowly than the α below 50°, but faster above 50°. Another familiar example is the sulphonation of naphthalene, which is slower at 80°, but faster at 160° in the β- than in the α-position, while the reverse applies to the hydrolysis of the corresponding sulphonic acids. Somewhat similar observations have been made for the bromination of naphthalene.[9] In all these cases, the energies of activation of α- and β-derivatives have closely similar values and the Arrhenius plots evidently have a cross-over point within the range of measurements, so that the isomer which is more reactive will depend on the temperature chosen for comparison. As had previously been pointed out,[2] these facts are in accord with simple valence-bond theory, which predicts a relatively small difference between the polarisability of the α- and the β-position of naphthalene, but are quantitatively in disagreement with molecular-orbital calculations which predict a larger difference between the two positions in naphthalene than between naphthalene and benzene.

For both α- and β-naphthylphenylallyl alcohols, the equilibria lie on the side of the 3-naphthyl-1-phenylallyl isomers, *i.e.*, those in which the naphthyl group is conjugated with the double bond. The equilibrium constants are larger for the α- than for the β-isomer, and the values of the free energy changes $-\Delta G_{30}$ are 205 and 35 cal./mole, respectively. The equilibrium constants decrease slightly with increasing temperature, but over the range studied (30—60°), the differences are almost within experimental error and do not justify a separate estimate of the enthalpy changes $-\Delta H$; these must be of the same order as, or smaller than, $-\Delta G$. The present results show that an ethylenic bond conjugates more strongly with a naphthyl than with a phenyl group, and more strongly in the α- than in the β-position, *i.e.*, in the sequence Ph < β-$C_{10}H_7$ < α-$C_{10}H_7$.

Previous equilibrium studies in the naphthalene field [10] comprise the reversible prototropic rearrangements of 1-phenyl-3-arylmethyleneazomethines,[10a] in which conjugation of an aryl nucleus with CH=N was shown to increase in the sequence α-$C_{10}H_7$ < Ph < β-$C_{10}H_7$ (but in which the equilibrating species presumably is anionic), and the reversible solvolysis of aryl chloromethyl derivatives,[10b] which is not significant for the present investigation. The only other relevant experiments appear to be those by Badger [11] who inferred from a study of rates of hydroxylation that in 1 : 2-diarylethylenes there is greater conjugation between an ethylenic bond and an α- than a β-naphthyl group. This is in agreement with the calculated bond orders [11] of the ethylenic linkage, which are an *inverse* measure of the conjugating effect of the aryl group and decrease in the sequence Ph (1·820) > β-naphthyl (1·814) > α-naphthyl (1·792).

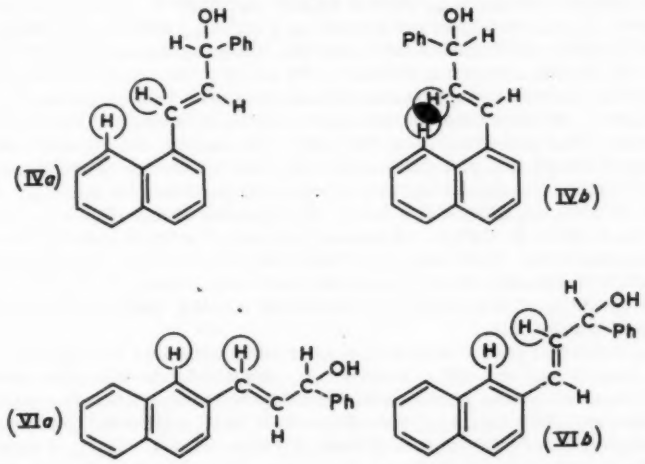
The conjugating properties of the α- and the β-positions in naphthalene were first discussed theoretically by Hückel [12] in 1932 and then by many other authors, particularly during recent years. The most precise calculations of the conjugation energies for the α- and the β-vinylnaphthalene system are those by Coulson and Longuet-Higgins,[13] which lead to (rounded) values of 7530 and 6890 cal./mole, to be compared with 6770 for the styryl system. The differences of 760 and 120 cal., respectively, are qualitatively, though not quantitatively, in agreement with the present results. It will be noted that the calculated figures are larger than the experimental ones by about the same factor (3·7, 3·4) in each case. The possibility that the molecular-orbital approximation exaggerates the difference in conjugating properties of the α- and the β-position in naphthalene cannot be excluded, but it seems probable that the lack of quantitative agreement is, at least partly, inherent in the particular features of the equilibrium system on which the experimental data are based. Thus, the free-energy difference between the two isomers may deviate

[9] Spryskov, *J. Gen. Chem.* (*U.S.S.R.*), 1947, **17**, 59; cf. Braude, *Ann. Reports*, 1949, **46**, 137.
[9] Sixma, *Rec. trav. chim.*, 1949, **68**, 925; Sixma and Wibaut, *ibid.*, 1950, **69**, 577.
[10] (*a*) Shoppee, *J.*, 1933, 37; (*b*) Dewar and Sampson, *J.*, 1956, 2789.
[11] Badger, *Nature*, 1950, **165**, 647; Coulson, *J.*, 1950, 2252.
[12] Hückel, *Z. Physik*, 1932, **76**, 636.
[13] Coulson and Longuet-Higgins, *Proc. Roy. Soc.*, 1947, **192**, *A*, 16.

somewhat from the resonance-energy difference owing to secondary structural effects due to the allyl alcohol grouping.

The possibility of special steric effects in the α-vinylnaphthalene derivatives must also be considered. Whereas in the β-vinylnaphthalene derivative both uniplanar conformations (VI*a* and VI*b*) are essentially free from strain and will be similar in energy content, in the α-vinylnaphthalene derivative one uniplanar conformation (IV*b*) is subject to severe steric interference between the 8-hydrogen atom of the aromatic ring and one of the hydrogen atoms attached to the vinyl group, so that the other unhindered uniplanar conformation (IV*a*), in which maximum resonance-stabilisation is not off-set by repulsion forces, will be preferred. In the anionotropic rearrangement, the initial conformation of the product will depend on that of the reactant, and it can easily be seen that of two

FIG. 2.



possible types of conformation of the starting alcohol, one will lead to the unhindered and the other to the hindered conformation of the isomer. This is tantamount to a decrease in resonance stabilisation in the transition state, as well as an increased loss in rotational freedom accompanying the rearrangement, and will result in a larger energy of activation and a smaller free energy gain. Both the relatively low rate of formation (k_1), and the relatively low rate of disappearance (k_{-1}), of the α-vinylnaphthalene system may thus be accounted for.

EXPERIMENTAL

Analytical data were determined in the organic microanalytical laboratory of this Department (Mr. F. H. Oliver and his staff). Some of the spectroscopic data were determined by Mrs. A. I. Boston using Hilger-Spekker and Unicam instruments. The spectrometric work on the naphthyl-phenylallyl alcohols was carried out with a Beckman instrument (see below).

1-α-*Naphthyl*-3-*phenylallyl Alcohol* (III) (with J. S. FAWCETT).—Freshly distilled cinnamaldehyde (66 g.) in ether (300 ml.) was added during 3 hr. to a stirred solution of 1-naphthylmagnesium bromide [from magnesium (12 g.) and 1-bromonaphthalene (103 g.)] in ether (500 ml.) under nitrogen at 10°. Stirring was continued for a further 3 hr., excess of saturated aqueous ammonium chloride was added, and the ether layer was separated, washed with water, dried ($Na_2SO_4 + K_2CO_3$), and evaporated under reduced pressure. Naphthalene (2 g., 3%) was separated from the solid product by sublimation in a vacuum and the residue (98 g., 75%) was crystallised from light petroleum, giving the *alcohol*, m. p. 66—67°, $\lambda_{max.}$ 2240, 2510, 2580, 2820, and 2910 Å (ε 85,000, 20,000, 22,400, 13,800, and 9900, respectively) in ethanol (Found: C, 87·4; H, 6·3. $C_{19}H_{16}O$ requires C, 87·7; H, 6·2%).

2-α-*Naphthylvinyl Phenyl Ketone* (VIII).—α-Naphthaldehyde [14] was stored as the hydrogen sulphite derivative.[15] The 2 : 4-dinitrophenylhydrazone had m. p. 251°, $\lambda_{max.}$ 3910 Å (ε 30,000) in chloroform (Coles and Dodds [16] give m. p. 254°).

A mixture of the aldehyde (8·5 g.), acetophenone (5·7 g.), ethanol (200 ml.), and 10% aqueous sodium hydroxide (25 ml.) was kept for 18 hr. at room temperature. The solution was acidified with dilute hydrochloric acid and extracted with benzene. The solvent was distilled off and a small amount of a solid *product*, which appears to be derived from the condensation of 2 molecules of acetophenone and 1 molecule of naphthaldehyde with the elimination of 1 molecule of water, was separated; it crystallised from methanol in colourless needles, m. p. 120° (Found: C, 85·4; H, 5·8. $C_{27}H_{22}O_2$ requires C, 85·7; H, 5·9%). The bulk of the reaction product was an oil which was chromatographed in benzene on alumina and then crystallised from benzene–light petroleum, giving pale yellow crystals (11·7 g.), m. p. 56—68°. After two recrystallisations from ethanol, the bulk of the material still melted over a range and appeared to show a double melting point, 72—77° and 84—88° (Gheorgiv and Matei [17] give m. p. 88° and state that the ketone is phototropic); it had $\lambda_{max.}$ 2650 (ε 19,000) and 3520 Å (ε 14,500) in ethanol. The 2 : 4-dinitrophenylhydrazone formed red crystals, m. p .45°, $\lambda_{max.}$ 4030 Å. (ε 30,000) in chloroform.

3-α-*Naphthyl*-1-*phenylallyl Alcohol* (IV).—(*a*) The foregoing ketone (1 g.) in ether (150 ml.) was treated with lithium aluminium hydride (0·36 g.) at −30°. After 1·5 hr., ethyl acetate (10 ml.) was added, followed by aqueous ammonium chloride. The organic layer was separated and dried (Na_2SO_4), the ether was removed under reduced pressure, and the residue was taken up in hot benzene–light petroleum (b. p. 60—80°). On cooling, the impure *alcohol* separated as a pale yellow oil (0·9 g.), b. p. 150° (bath temp.)/10^{-4} mm., which was chromatographed in benzene on neutral alumina; it did not solidify at room temperature and had $\lambda_{max.}$ 2900 (ε 9300) and 2970 Å (ε 10,000), $\lambda_{infl.}$ 2560 Å (ε 8000) in 60% aqueous dioxan (Found: C, 87·8; H, 6·4. $C_{19}H_{16}O$ requires C, 87·7; H, 6·2%). It gave no precipitate on treatment with Brady's reagent and on rearrangement with hydrochloric acid afforded about 80% of the equilibrium mixture of the α-naphthyl-phenylallyl alcohols, as determined spectrometrically (see below). The oil thus contains *ca.* 80% of 3-α-naphthyl-1-phenylallyl alcohol, probably admixed with 3-α-naphthyl-1-phenylpropan-1-ol.

(*b*) 2-α-Naphthylvinyl phenyl ketone (3·6 g.) in ether (100 ml.) was treated with lithium aluminium hydride (0·5 g.) at −20°. Aqueous ammonium chloride was added and the product was worked up as above, giving 2-α-*naphthylethyl phenyl ketone* as a pale yellow oil (3·0 g., 83%), b. p. 120° (bath-temp.)/10^{-4} mm., $\lambda_{max.}$ 2240, 2510, 2580, 2810, and 2900 Å (ε 55,000, 9500, 9500, 8000, and 8000, respectively) in ethanol (Found: C, 87·6; H, 6·4. $C_{19}H_{16}O$ requires C, 87·7; H, 6·2%). The 2 : 4-*dinitrophenylhydrazone* crystallised from pyridine–ethyl acetate in orange needles, m. p. 227—228°, $\lambda_{max.}$ 3840 Å (ε 26,500) in chloroform (Found: C, 65·6; H, 5·0; N, 12·7. $C_{25}H_{20}O_4N_4$ requires C, 68·2; H, 4·6; N, 12·7%).

(*c*) (With J. S. Fawcett.) 2-α-Naphthylvinyl phenyl ketone (5 g.) in ether (25 ml.) and benzene (25 ml.) was treated with lithium aluminium hydride (0·4 g.) in ether (50 ml.) at 0°. Isolation of the product as above gave 3-α-*naphthyl*-1-*phenylpropan*-1-*ol* (2·5 g.), b. p. 120° (bath-temp.)/10^{-4} mm. (Found: C, 86·8; H, 7·2. $C_{19}H_{18}O$ requires C, 87·0; H, 6·9%). The *p*-*nitrobenzoate* had m. p. 123—125° [from light petroleum (b. p. 100—120°)] (Found: C, 76·2; H, 5·2; N, 3·5. $C_{26}H_{21}O_4N$ requires C, 75·9; H, 5·1; N, 3·4%).

2-*Acetylnaphthalene*.—2-Cyanonaphthalene (9·5 g.) in ether (100 ml.) was added to methylmagnesium iodide [from magnesium (1·6 g.) and methyl iodide (9·3 g.)] in ether (65 ml.), and the mixture was refluxed for 1 hr. under nitrogen. After cooling, excess of 2N-hydrochloric acid was added, and the ether layer was separated, washed, and evaporated. The dark brown solid product was chromatographed on alumina in benzene and then crystallised from light petroleum (b. p. 60—80°), giving the colourless ketone (6·6 g., 63%), m. p. 48° (Stobbe [18] gives m. p. 51·5°). The mother-liquors, with Brady's reagent, gave the 2 : 4-dinitrophenylhydrazone (2·2 g., corresponding to a further 10% yield of ketone), m. p. 231°, which after chromatography on alumina in benzene–ethyl acetate and crystallisation from ethyl acetate–carbon tetrachloride formed bright red needles, m. p. 251—252°, $\lambda_{max.}$ 3850 Å (ε 30,000) in chloroform (Found: C, 61·4; H, 4·1; N, 15·6. $C_{18}H_{14}O_4N_4$ requires C, 61·7; H, 4·0; N, 16·0%).

[14] Angyal, Tetaz, and Wilson, *Org. Synth.*, 1950, **30**, 67.
[15] Cf. Bamberger and Looter, *Ber.*, 1888, **21**, 259.
[16] Coles and Dodds, *J. Amer. Chem. Soc.*, 1938, **60**, 853.
[17] Gheorghiu and Matei, *Gazzetta*, 1943, **73**, 65; *Chem. Abs.*, 1947, **41**, 2719.
[18] Stobbe, *Annalen*, 1911, **380**, 95.

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β-*Naphthyl Styryl Ketone* (VII).—(*a*) A solution of the foregoing ketone (2·6 g.) and benzaldehyde (1·6 g.) in 85% ethanol (55 ml.) containing sodium hydroxide (0·5 g.) was kept at room temperature. A first crop (3·0 g., 75%), m. p. 102°, was collected after 2 hr. and a second (0·2 g., 5%), m. p. 97°, after a further 2 hr. The two crops were combined and after one crystallisation from ethanol formed pale yellow needles, m. p. 102°, $\lambda_{max.}$ 2510 (ε 14,700), 2580 (ε 14,700), and 3130 Å (ε 19,300) in dioxan (Matei [19] gives m. p. 104°).

(*b*) A solution of 2-acetylnaphthalene (6·6 g.) and benzaldehyde (4·2 g.) in dry ethyl acetate (60 ml.) was saturated with dry hydrogen chloride. After 42 hr., during which considerable darkening occurred, the solvent was removed under reduced pressure and the residue dissolved in benzene. The benzene solution was thoroughly washed with aqueous sodium hydrogen sulphite, water, dilute aqueous potassium hydroxide, and again water, dried (Na_2SO_4), and passed through alumina. The eluate was evaporated and the solid residue was fractionally sublimed at 100° (bath-temp.)/10^{-4} mm. Unchanged 2-acetylnaphthalene (3·5 g., 53%) sublimed first, followed by β-naphthyl styryl ketone which was crystallised from ethanol, giving pale yellow needles (1·1 g., 23%), m. p. 102°, undepressed on admixture with the specimen obtained as under (*a*).

1-β-*Naphthyl-3-phenylallyl Alcohol* (V).—Lithium aluminium hydride (0·28 g.) in ether (100 ml.) was added during 20 min. to a stirred solution of the foregoing ketone (3·7 g.) in ether (200 ml.) and benzene (60 ml.) at −20°. After a further 30 min., excess of aqueous ammonium chloride was added, the upper layer was separated, and the aqueous layer extracted with ether. The combined ether–benzene solutions were washed with water, dried (Na_2SO_4), and evaporated under reduced pressure. The solid residue was crystallised once from benzene–light petroleum, giving the *alcohol* as colourless needles (1·9 g., 51%), m. p. 78°, $\lambda_{max.}$ 2510 (ε 27,000) and 2640 Å (ε 26,000) in ethanol (Found: C, 87·5; H, 6·3. $C_{19}H_{16}O$ requires C, 87·7; H, 6·2%). The mother-liquors deposited more of the alcohol (0·5 g., 14%) as fluffy needles, m. p. 75°, together with colourless flakes of β-*naphthyl phenethyl ketone* (0·55 g., 15%). The latter were separated manually and after one crystallisation from benzene–light petroleum had m. p. 92—93°, $\lambda_{max.}$ 2480, 2800, 2900, 3280, and 3370 Å (ε 52,000, 10,500, 8900, 1200, and 1200, respectively) in chloroform (Found: C, 87·1; H, 6·0. $C_{19}H_{16}O$ requires C, 87·7; H, 6·2%). The ketone gave an immediate precipitate with Brady's reagent and its m. p. was depressed to 74—76° on admixture with β-naphthyl styryl ketone.

An attempt to prepare the alcohol from cinnamaldehyde and β-naphthylmagnesium bromide, under conditions similar to those used above with α-naphthylmagnesium bromide, gave only 2 : 2′-dinaphthyl, m. p. 178° (Meyer and Hofman [20] give m. p. 181°), together with intractable, high-boiling products.[21]

β-*Naphthaldehyde*.—Lithium aluminium hydride (0·9 g.) in ether (80 ml.) was added during 20 min. to a stirred solution of 2-cyanonaphthalene (10 g., m. p. 64—66°, prepared analogously to *o*-toluonitrile [22]) in ether (100 ml.) at 0°. After a further 80 min., the buff-coloured precipitate was dissolved by adding 2N-sulphuric acid (200 ml.). Stirring was continued for 30 min. and the ethereal layer was then separated, washed with water, dried (Na_2SO_4), and evaporated. The product was purified *via* the sodium hydrogen sulphite derivative and by crystallisation from aqueous alcohol, giving β-naphthaldehyde (6·7 g., 65%), m. p. 62—63° (Shoppee [10a] gives m. p. 59°). The bright red 2 : 4-dinitrophenylhydrazone, after chromatography on alumina in benzene–ethyl acetate and crystallisation from ethyl acetate, had m. p. 262°, $\lambda_{max.}$ 3840 Å (ε 32,000) in chloroform (Pickering and Smith [23] give m. p. 270°).

2-β-*Naphthylvinyl Phenyl Ketone* (VIII).—(*a*) Dry hydrogen chloride was passed for 30 min. through a solution of β-naphthaldehyde (4·3 g.) and acetophenone (2·8 g.) in dry ethyl acetate (100 ml.). The solution was then kept in a closed flask at room temperature for 42 hr., during which there was copious separation of pale yellow crystals. The solvent was removed under reduced pressure and the product crystallised from benzene, giving 2-β-*naphthylvinyl phenyl ketone* (5·3 g., 76%), m. p. 154°, $\lambda_{max.}$ 2800 (ε 20,000) and 3280 Å (ε 24,000) in ethanol (Found: C, 88·5; H, 5·8. $C_{19}H_{14}O$ requires C, 88·3; H, 5·5%).

[19] Matei, *Ann. Sci. Univ. Jassy*, 1943, **29**, 17.
[20] Meyer and Hofman, *Monatsh.*, 1916, **37**, 708.
[21] Cf. Lovenich and Loesser, *Ber.*, 1927, **60**, 320; Gilman, Zoellner, and Didsey, *J. Amer. Chem. Soc.*, 1929, **51**, 1579.
[22] *Org. Synth.*, Coll. Vol. I, 1941, p. 514.
[23] Pickering and Smith, *Rec. Trav. chim.*, 1950, **69**, 535.

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(*b*) 10% Aqueous sodium hydroxide (10 ml.) was added to a solution of β-naphthaldehyde (3·3 g.) and acetophenone (2·2 g.) in ethanol (100 ml.). After 2 hr. at room temperature the crystalline precipitate was filtered off. The filtrate was kept for a further 15 hr. and diluted with water, and the precipitate was collected. The combined solid products were chromatographed on alumina in benzene and finally crystallised from ethanol, giving the ketone as very pale yellow crystals (2·2 g., 40%), m. p. and mixed m. p. 154°.

3-β-*Naphthyl*-1-*phenylallyl Alcohol* (VI).—Lithium aluminium hydride (0·3 g.) in ether (150 ml.) was gradually added, with stirring, to the foregoing ketone (4 g.) in ether (90 ml.) and benzene (40 ml.) at −20°. Stirring was continued for 30 min., excess of saturated aqueous ammonium chloride was added, and the ether layer was separated, washed with water, dried (Na_2SO_4), and evaporated under reduced pressure. The solid product (4·0 g.) crystallised from benzene–light petroleum in colourless tufts (2·6 g., 65%), m. p. 76°, $\lambda_{max.}$ 2490, 2570, 2770, 2870, and 2980 Å (ε 53,000, 49,000, 16,000, 19,500, and 17,000, respectively) in ethanol–dioxan (20 : 1) (Found: C, 88·0; H, 6·3. $C_{19}H_{16}O$ requires C, 87·7; H, 6·2%).

Conversion of Benzonitrile into Benzaldehyde.—65% Lithium aluminium hydride (2·9 g., 0·25 mol.) was added gradually to a stirred solution of benzonitrile (21·1 g.) in dry ether (200 ml.) at −5°. Ethyl acetate (1 ml.) was then added to destroy excess of hydride, followed by 2N-sulphuric acid (200 ml.), and the whole stirred for 30 min. at room temperature. The ether layer was separated, the aqueous layer was extracted with ether, and the combined ether solutions were shaken with saturated aqueous sodium metabisulphite, all these operations being conducted under nitrogen. The bisulphite compound (22·7 g., 50%; 73% on unrecovered benzonitrile) was filtered off, and a portion was converted by Brady's reagent into benzaldehyde 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 233°. Distillation of the ether solution yield unchanged benzonitrile (7·0 g.), b. p. 68°/13 mm., n_D^{18} 1·5300.

Kinetic Measurements.—These were carried out with a Beckman D.U. spectrophotometer, provided with a mounting block and a specially constructed cell-holder both in a thermostat. The temperature inside the absorption cells was within ±0·05° between room temperature and 50°.

The reaction medium was prepared from 59 ml. of dioxan and 10·2 ml. of 0·1N-hydrochloric acid, made up to 100 ml. with water. The composition of this medium is such that, after addition of 0·15 ml. of dioxan to 2·45 ml., it becomes 60% (by vol.) aqueous dioxan–0·01M-hydrogen chloride. Stock solutions of the allyl alcohols were prepared by weighing out an appropriate amount (usually 2—20 mg.) and dissolving it in 10 ml. of dioxan. Dioxan was purified by prolonged refluxing over sodium, followed by fractionation; only cuts with an extinction of less than 0·5 at 2550 Å in a 1 cm. cell (corresponding to a benzene content of less than 0·02%) were used. All vessels were very thoroughly cleaned with chromic acid, washed with conductivity water and then redistilled spectroscopically pure ethanol, and dried at 100°; these precautions were essential to eliminate effects which appear to be due to traces of alkali adhering to the surfaces.

2·50 Ml. of medium were introduced into the comparison cell and 2·45 ml. into the solution cell, a lid was placed on the solution cell, both cells were placed in position, and a thermometer was inserted into the comparison cell through a hole provided in the cover slide. When the desired temperature had been reached, the instrument was balanced with the comparison cell in the light beam, the thermometer was withdrawn, and the lid was transferred to the comparison cell. 0·05 Ml. of stock solution was next added to the solution cell from an "Agla" microsyringe, the solution was mixed by ten rapid up-and-down strokes with a small pre-warmed glass stirrer, and the initial reading was immediately taken with the solution cell in the beam. Further readings were taken at appropriate intervals; if the half-time of the rearrangement exceeded 10 min., the contents of the cells were later transferred to stoppered flasks immersed in the thermostat bath to allow the reaction equilibrium to be reached, and then returned to the pre-warmed cells for the final reading.

The concentrations of alcohol were so chosen as to give a final E value of 0·5—0·7 at the wavelength employed. In general, the 3000 Å region where the alcohols exhibit maxima with ε *ca.* 10,000 was found the most convenient; in the 2500 Å region where the maxima are of higher intensity (ε *ca.* 50,000), fluorescence effects are marked [24] and the stronger solvent absorption reduces the total light flux and consequently lowers the accuracy. Under optimum conditions, E readings were reproducible to about ±0·002.

First-order rate-constants were calculated from $k = (2{\cdot}3/t) \log [(a - x_0)/(a - x)]$ where x_0

[24] Braude, Fawcett, and Timmons, *J.*, 1950, 1019.

and a are the initial and the final reading and x is the reading at time t; the estimated accuracy is $\pm 2\%$. Equilibrium constants were calculated from $K = (a - x_0)a'/(x_0' - a')a$ where x_0' and a' are the initial and the final readings for the isomeric alcohol at a comparable concentration. Energies of activation were computed graphically; the plots of k against $1/T$ were satisfactorily linear in each case. Entropies of activation were calculated from $\Delta S = 2{\cdot}3\boldsymbol{R} \log k + (E_A - \boldsymbol{RT})/T - 2{\cdot}3\boldsymbol{R} \log (\boldsymbol{RT}/\boldsymbol{Nh}) = 4{\cdot}6 \log k + (E_A - \boldsymbol{RT})/T - 59$ after conversion of k's (in min.$^{-1}$ and for 0·01M-acid solutions) into specific k's (in sec.$^{-1}$ and for M-acid solutions).

Six representative runs at 30° are recorded.

(i) Rearrangement of (III) ($0{\cdot}1474 \times 10^{-4}$M).

Time (min.)	0	13·1	18·1	20·5	26·7	29·3	34·5	38·3	45·5	54·2	64·9	1200
E at 3180 Å	0·062	0·174	0·210	0·228	0·270	0·284	0·314	0·331	0·365	0·401	0·436	0·609
10^4k (min.$^{-1}$)	—	175	174	177	179	178	179	177	177	178	177	—

Mean = 177

(ii) Rearrangement of (IV) ($0{\cdot}1461 \times 10^{-4}$M).

Time (min.)...	0	14·4	17·2	20·8	26·2	28·7	31·9	34·5	41·5	52·7	930	
E at 3180 Å	0·800	0·734	0·720	0·711	0·690	0·681	0·671	0·661	0·648	0·619	0·488	
10^4k (min.$^{-1}$)	—	165	172	162	166	167	167	171	161	165	—	Mean = 166

(iii) Rearrangement of (V) ($0{\cdot}156 \times 10^{-4}$M).

Time (min.)...	0	10·9	12·1	13·3	15·8	17·1	18·3	20·6	24·9	27·8	300	
E at 2490 Å	0·435	0·477	0·481	0·486	0·494	0·499	0·501	0·507	0·518	0·521	0·618	
10^4k (min.$^{-1}$)	—	240	240	246	247	251	245	243	243	228	—	Mean = 243

(iv) Rearrangement of (V) ($0{\cdot}508 \times 10^{-4}$M).

Time (min.)	0	9·4	11·5	15·2	18·1	22·2	25·2	28·2
E at 3000 Å	0·121	0·190	0·203	0·226	0·242	0·262	0·275	0·286
10^4k (min.$^{-1}$)	—	260	259	264	265	264	263	259
Time (min.)	35·2	38·0	42·1	45·1	49·0	1020		
E at 3000 Å	0·314	0·322	0·334	0·342	0·353	0·439		
10^4k (min.$^{-1}$)	265	263	263	263	267	—	Mean = 263	

(v) Rearrangement of (VI) ($0{\cdot}156 \times 10^{-4}$M).

Time (min.)	0	14·2	14·9	16·3	18·0	21·8	25·2	32·0	33·1	310	
E at 2490 Å	0·729	0·691	0·689	0·687	0·684	0·679	0·669	0·659	0·655	0·602	
10^4k (min.$^{-1}$)	—	250	254	246	243	230	254	250	264	—	Mean = 249

(vi) Rearrangement of (VI) ($0{\cdot}508 \times 10^{-4}$M).

Time (min.)	0	8·3	10·8	12·1	15·4	17·5	19·5	22·6
E at 3000 Å	0·704	0·650	0·634	0·631	0·612	0·602	0·596	0·581
10^4k (min.$^{-1}$)	—	251	259	243	251	251	242	248
Time (min.)	24·9	28·5	30·5	37·0	42·4	1080		
E at 3000 Å	0·572	0·559	0·530	0·530	0·516	0·417		
10^4k (min.$^{-1}$)	248	247	247	252	251	—	Mean =	249

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11. *Purines, Pyrimidines, and Glyoxalines. Part XI.* Some Oxazolidino- and Thiazolidino-[2 : 3-a]pyrimidines, and a Synthesis of Thymidine.*

By G. Shaw and R. N. Warrener.

Oxazolidino- and thiazolidino-[2 : 3-*a*]pyrimidines have been prepared by the reaction of 1-substituted hydroxyalkyl-uracils and -thiouracils respectively with methanesulphonyl chloride or toluene-*p*-sulphonyl chloride, and cyclisation of the resulting esters. Some properties of these compounds have been investigated and the method has been adapted to a synthesis of thymidine from 5-methyl-2-thiouridine.

When 2′-O-*p*-toluenesulphonyl or -methanesulphonyl derivatives of uridine and related pyrimidine ribofuranosides are heated with bases, the reaction $C_{(2)}$–OH + $C_{(2')}$–O·SO_2R ⟶ $C_{(2)}$–O–$C_{(2')}$ + R·SO_2·OH occurs with liberation of the sulphonic acid and formation of a *O*^{2} : 2′-*cyclo*nucleoside with simultaneous inversion of configuration at $C_{(2')}$. The *cyclo*-nucleosides can be hydrolysed to β-D-arabinofuranosides and this property has been used in the preparation of spongouridine [1] (1-β-D-arabinofuranosyluracil) and spongothymidine [2] (1-β-D-arabinofuranosylthymine) from uridine and 5-methyluridine respectively. *cyclo*-Nucleoside formation also provides conclusive proof of the β-configuration at the glycosidic centre of the above ribofuranosides. The analogous but hitherto unknown *S*^{2} : 2′-*cyclo*-thiouridines (X) by similar reactions should lead to the 2′-deoxy-2′-thioarabinofuranosyl-uracils series which by desulphurisation would be a source of 2′-deoxyribofuranosyl-uracils.

We examined initially some simpler compounds. 1-(Hydroxyalkyl)uracils and related compounds are now readily available by methods outlined in earlier papers, from primary amines and appropriate linear precursors of uracils or 2-thiouracils.[3] Reaction of ethanolamine and 2-hydroxypropylamine with the ethoxymethylene derivative (I) gave the 2′-hydroxyalkyluracils (II; R = CN, R′ = H or Me, R″ = H) which were readily converted into the sulphonates (II; R = CN, R′ = H and Me, R″ = Me·SO_2 or *p*-Me·C_6H_4·SO_2). When either ester was heated in acetone with triethylamine an initial deep magenta-coloured solution was obtained which slowly faded as the oxazolidino-pyrimidines (III; R = CN, R′ = H or Me) separated from the solution. With methanolic ammonia the cyano-compound (III; R = CN, R′ = H) gave the *iso*cytosine derivative (IV), and the same compound was also obtained from the ester (II; R = CN, R′ = H, R″ = *p*-Me·C_6H_4·SO_2) and methanolic ammonia.

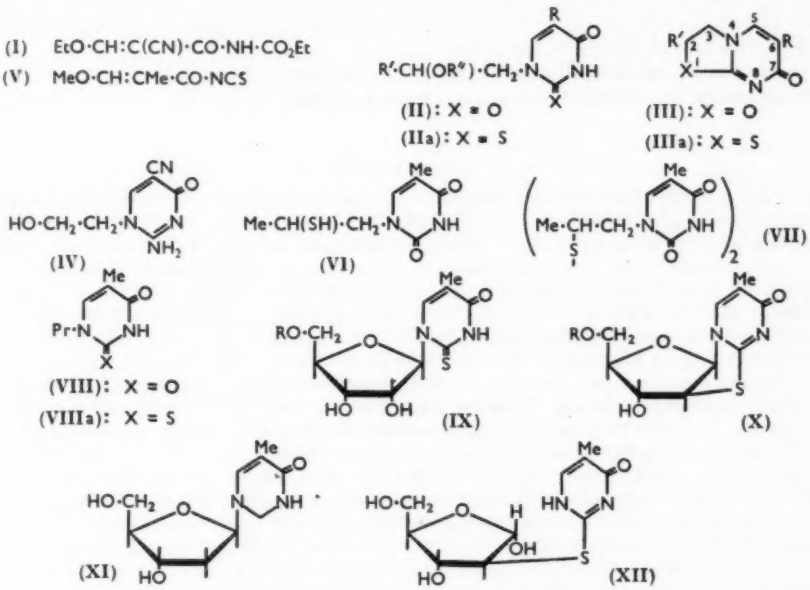
In a similar manner, reaction of ethanolamine and 2-hydroxypropylamine with the acyl *iso*thiocyanate (V) readily gave the thiothymines (IIa; R = Me, R′ = H or Me, R″ = H). These with methanesulphonyl chloride in pyridine at room temperature gave directly the thiazolidinopyrimidines (IIIa; R = Me, R′ = H or Me); intermediate *O*-methanesulphonyl derivatives could not be isolated. A positive reaction for the thiol group with sodium nitroprusside was rapidly obtained when the cyclic compound (IIIa; R = R′ = Me) was warmed with aqueous sodium hydroxide, and the thiol (VI) was readily isolated from the reaction mixture. Attempts to desulphurise this compound proved troublesome. With W7 Raney nickel catalyst or with iodine in aqueous alkali, the disulphide (VII) was obtained; however, reaction with W2 nickel catalyst gave 1-propylthymine (VIII), which was also prepared by the reaction of the *iso*thiocyanate (V) with propylamine and desulphurisation of the resulting 1-propyl-2-thiothymine (VIIIa) with chloroacetic acid.

* Part X, *J.*, 1958, 2299.

[1] Brown, Todd, and Varadarajan, *J.*, 1956, 2388.
[2] Fox, Yung, and Bendich, *J. Amer. Chem. Soc.*, 1957, **79**, 2775.
[3] (*a*) Shaw, *J.*, 1955, 1834; Shaw and Warrener, *J.*, 1958, (*b*) **153**, (*c*) 157.

XUM

Adaptation of these reactions to a synthesis of thymidine (XI) required the preparation of 5-methyl-S^2 : 2′-*cyclo*thiouridine (X; R = H). Similar O^2 : 2′-*cyclo*uridines have been prepared by toluene-*p*-sulphonylation or methanesulphonylation of 5′-*O*-acetyluridine or 5-methyl-5′-*O*-trityluridine and cyclisation of the esters with ammonia;[1,2] in these experiments, no evidence for sulphonylation at the 3′-hydroxyl group was recorded.



5-Methyl-2-thiouridine[3d] (IX; R = H) in pyridine readily gave a good yield of crystalline 5′-*O*-triphenylmethyl derivative (IX; R = CPh_3), the position of the triphenylmethyl group appearing certain by analogy with similar compounds prepared from uridine and 5-methyluridine. Our material also gave a positive test for a vicinal glycol with the starch–periodate reagent but this is of doubtful diagnostic value for thiouracil derivatives in which the sulphur appears to reduce periodate.

The ether (IX; R = CPh_3) with methanesulphonyl chloride in pyridine gave a solid which from its elementary analysis and ultraviolet absorption spectrum, similar to that of the analogue (IIIa; R = R′ = Me), was undoubtedly the *cyclo*thionucleoside (X; R = CPh_3). Fox, Yung, and Bendich[2] obtained a similar solid by methanesulphonylation of 5-methyl-5′-*O*-trityluridine, but from a low sulphur content concluded that only 25% of esterification had occurred. Since an excess of methanesulphonyl chloride was used, this conclusion appears unlikely and we suggest that this substance may have been a mixture of the 2′-*O*-methanesulphonyl derivative and the corresponding *cyclo*nucleoside.

Hydrolysis of the ether (X; R = CPh_3) with dilute acid gave triphenylmethanol and a syrup whose ultraviolet absorption was very similar to that of compound (IIIa; R = R′ = Me), suggesting that it was largely the *cyclo*-compound (X; R = H), and this was confirmed by its further reactions. When the syrup was warmed with dilute sodium hydroxide solution, the solution soon gave a positive thiol test with sodium nitroprusside, and the ultraviolet absorption changed to that of a simple uracil derivative. When the syrup was warmed with dilute sodium hydroxide solution in the presence of W2 Raney nickel, the solution soon gave strong positive tests for 2-deoxy-sugars with the Dische and the cysteine–sulphuric acid reagent. Paper chromatograms of this solution showed the

presence of thymidine as an absorbing spot accompanied by two other spots, all three giving a positive test with the cysteine spray. A small amount of crystalline thymidine (XI) was isolated and its identity confirmed by comparison with an authentic specimen. The nature of the two cysteine-positive compounds which accompanied the thymidine is not clear: one of them gave tests for a reducing sugar and had the same R_F value as 2-deoxyribose—the formation of 2-deoxyribose would be readily accounted for if fission at the glycosidic link (X; R = H) is a competing reaction, leading to (XII), desulphurisation of which would give the free sugar.

The formation of thymidine, although only of academic value in its present form, conclusively proves the β-configuration assigned to 5-methyl-2-thiouridine.

Experimental

5-Cyano-1-2′-hydroxyethyluracil.—2-Hydroxyethylamine (1·2 ml.) was added to a suspension of α-cyano-β-ethoxy-*N*-ethoxycarbonylacrylamide [3] (2·12 g.) in water (15 ml.), and the mixture heated on a water-bath for 5 min. The clear solution obtained was cooled and acidified with hydrochloric acid, to precipitate *5-cyano-1-2′-hydroxyethyluracil* (1·66 g.) which recrystallised from ethanol as needles, m. p. 194° (Found: C, 46·4; H, 4·1; N, 23·0. $C_7H_7O_3N_3$ requires C, 46·4; H, 3·9; N, 23·2%), $\lambda_{max.}$ 280 mμ (ε 12,950), $\lambda_{min.}$ 242 mμ (ε 1150) in water.

*5-Cyano-1-2′-toluene-*p*-sulphonyloxyethyluracil.*—A solution of the foregoing uracil (5·91 g.) and toluene-*p*-sulphonyl chloride (6·86 g.) in dry pyridine (10 ml.) was set aside at room temperature overnight, then treated with ice-water (200 ml.) and kept at 0° for 2 days, to give a crystalline precipitate. This was washed with ethanol (3 × 10 ml.) and ether (2 × 10 ml.), giving *5-cyano-1-2′-toluene-*p*-sulphonyloxyethyluracil* (5·6 g.) which recrystallised from a large volume of ethanol as needles, m. p. 238—240° (Found: C, 50·1; H, 4·05; N, 12·45. $C_{14}H_{13}O_5N_3S$ requires C, 50·15; H, 3·9; N, 12·5%). In a similar manner, the hydroxyethyluracil (1 g.) and methanesulphonyl chloride (0·46 ml.) in pyridine (7·5 ml.) afforded *5-cyano-1-2′-methanesulphonyloxyethyluracil* (1·09 g.), needles (from much methanol), m. p. 207° (Found: C, 37·3; H, 3·45; N, 16·15. $C_8H_9O_5N_3S$ requires C, 37·05; H, 3·5; N, 16·2%).

6-Cyano-7-oxo-oxazolidino[2 : 3-a]pyrimidine.—A solution of the foregoing toluene-*p*-sulphonate (1·5 g.) in acetone (75 ml.) containing triethylamine (4 ml.) was boiled under reflux for 2 hr. The mixture initially assumed a deep magenta colour which gradually faded, and a crystalline precipitate separated. The *cyclic compound* (0·62 g.) was sulphur-free and recrystallised from water as needles, m. p. 360° (Found: C, 51·9; H, 3·3; N, 25·5. $C_7H_5O_2N_3$ requires C, 51·55; H, 3·1; N, 25·75%), $\lambda_{max.}$ 277 (ε 7850), 227 mμ (ε 7300), $\lambda_{min.}$ 249 mμ (ε 2500) in water. The same substance (0·218 g.) was similarly prepared from the methanesulphonyl derivative (0·4 g.), acetone (50 ml.), and triethylamine (2 ml.).

*5-Cyano-1-2′-hydroxyethyl*isocytosine.—A suspension of the above-mentioned toluene-*p*-sulphonate (0·5 g.) in methanol (50 ml.) gave a clear red solution when treated with saturated methanolic ammonia (50 ml.). The solution was set aside for 16 hr., the red colour fading. Evaporation then gave *5-cyano-1-2′-hydroxyethyl*isocytosine (0·19 g.) which separated from water as needles, m. p. 248° (Found: C, 46·45; H, 4·4; N, 30·65. $C_7H_8O_2N_4$ requires C, 46·65; H, 4·5; N, 31·1%), $\lambda_{max.}$ 277 mμ (ε 8200), $\lambda_{min.}$ 252 mμ (ε 3600) in water. The same compound (0·084 g.) was similarly obtained from the foregoing cyclic compound (0·1 g.) and methanolic ammonia.

5-Cyano-1-2′-hydroxypropyluracil.—A solution of α-cyano-β-ethoxy-*N*-ethoxycarbonylacrylamide (2·5 g.) in water (15 ml.) containing 2-hydroxypropylamine (2 g.) was heated on a water-bath for 5 min. The cooled solution was acidified with 10N-hydrochloric acid, then set aside for a few hr. A crystalline precipitate separated. *5-Cyano-1-2′-hydroxypropyluracil* (2·3 g.) recrystallised from ethanol as prisms, m. p. 223° (Found: C, 49·2; H, 4·65; N, 21·4. $C_8H_9O_3N_3$ requires C, 49·25; H, 4·65; N, 21·55%), $\lambda_{max.}$ 280 mμ (ε 14,900), $\lambda_{min.}$ 240 mμ (ε 3250) in water.

5-Cyano-1-2′-methanesulphonyloxypropyluracil.—The foregoing uracil (1 g.) in dry pyridine (7·5 ml.) at 0° was treated with methanesulphonyl chloride (0·44 ml.), and the solution set aside at room temperature for 24 hr. Excess of acid chloride was decomposed by addition of a few drops of water to the mixture which was then kept for 30 min., and treated with more water (25 ml.) to precipitate *5-cyano-1-2′-methanesulphonyloxypropyluracil* (1·13 g.). This

separated from methanol as prisms, m. p. 212° (Found: C, 39·85; H, 3·95; N, 15·25. $C_9H_{11}O_3N_3S$ requires C, 39·55; H, 4·05; N, 15·4%). Similarly the foregoing uracil (1·95 g.), pyridine (10 ml.), and toluene-*p*-sulphonyl chloride (2 g.) gave *5-cyano-1-2′-toluene-p-sulphonyloxypropyluracil* (2·7 g.), plates (from ethanol), m. p. 208° (Found: C, 51·6; H, 4·55; N, 12·0. $C_{15}H_{15}O_5N_3S$ requires C, 51·6; H, 4·35; N, 12·05%).

6-Cyano-2-methyl-7-oxo-oxazolidino[2 : 3-a]*pyrimidine.*—A solution of the last-mentioned toluene-*p*-sulphonate (2 g.) in acetone (50 ml.) and triethylamine (4 ml.) was boiled under reflux for 2 hr. during which crystals slowly separated. The *cyclic compound* (0·36 g.) was collected and recrystallised from water as plates, m. p. 248° (Found: C, 54·35; H, 4·15; N, 23·75. $C_8H_7O_2N_3$ requires C, 54·25; H, 4·0; N, 23·7%), $\lambda_{max.}$ 227 (ε 7900), 276 mμ (ε 8250), $\lambda_{min.}$ 249 mμ (ε 2900) in water. A further quantity of the compound (0·5 g.) was obtained by evaporation of the acetone solution.

1-2′-Hydroxyethyl-5-methyl-2-thiothymine.—A vigorous reaction occurred when β-methoxy-α-methylacryloyl *iso*thiocyanate[3b] (1·6 g.) was added to 2-hydroxyethylamine (1·2 g.) in water (5 ml.). The cooled solution was acidified and the precipitated solid collected. *1-2′-Hydroxyethyl-5-methyl-2-thiothymine* (1·3 g.) separated from ethanol as needles, m. p. 204° (Found: C, 45·45; H, 5·2; N, 14·8. $C_7H_{10}O_2N_2S$ requires C, 45·15; H, 5·4; N, 15·05%), $\lambda_{max.}$ 275 mμ (ε 15,380), $\lambda_{min.}$ 243 mμ (ε 4240).

6-Methyl-7-oxothiazolidino[2 : 3-a]*pyrimidine.*—The thiothymine (0·95 g.) in pyridine (5 ml.) with methanesulphonyl chloride (0·6 g.) was set aside for 24 hr., and the resulting crystals were collected. The *cyclic compound* (0·4 g.) separated from water as prisms, m. p. 262° (Found: C, 49·9; H, 4·75; N, 16·65. $C_7H_6ON_2S$ requires C, 50·0; H, 4·8; N, 16·65%), $\lambda_{max.}$ 228 mμ (ε 20,500), $\lambda_{infl.}$ 260 mμ (ε 6700) in water.

1-2′-Hydroxypropyl-2-thiothymine.—2-Hydroxypropylamine (2·5 g.) in ether (10 ml.) was added to β-methoxy-α-methylacryloyl *iso*thiocyanate (4·4 g.) in ether (30 ml.); a vigorous reaction occurred and a solid separated. This was heated with 2N-sodium hydroxide (12 ml.) on a water-bath for 5 min., then cooled and acidified to give *1-2′-hydroxypropyl-2-thiothymine* (4·05 g.) recrystallising from ethanol as prisms, m. p. 191° (Found: C, 47·9; H, 6·25; N, 13·55. $C_8H_{12}O_2N_2S$ requires C, 48·0; H, 6·05; N, 14·0%), $\lambda_{max.}$ 275 mμ (ε 16,100), $\lambda_{min.}$ 245 mμ (ε 5200) in water. A solution of the thiothymine (1 g.) in pyridine (3 ml.) containing benzoyl chloride (1 ml.) was set aside for 3½ hr., then acidified with hydrochloric acid to precipitate a gum which solidified when rubbed with ethanol; *1-2′-benzoyloxypropyl-2-thiothymine* (0·45 g.) separated from ethanol as needles, m. p. 202° (Found: C, 59·3; H, 5·1; N, 9·45. $C_{15}H_{16}O_3N_2S$ requires C, 59·2; H, 5·3; N, 9·2%). The benzoate (0·33 g.) in ethanol (30 ml.) and sodium ethoxide in ethanol (1·04 ml., 5%) were set aside for 20 hr., then evaporated, and the residue was treated with water (5 ml.) and extracted with ether. The aqueous solution was acidified, 1-2′-hydroxypropyl-2-thiothymine (0·195 g.), m. p. and mixed m. p. 186°, being precipitated.

2 : 6-Dimethyl-7-oxothiazolidino[2 : 3-a]*pyrimidine.*—Methanesulphonyl chloride (2·5 ml.) was added to 1-2′-hydroxypropyl-2-thiothymine (5·3 g.) in pyridine (20 ml.) at 0°, and the solution set aside for 24 hr. A crystalline precipitate was collected and washed with pyridine (2 × 3 ml.). The *cyclic compound* (1·75 g.) recrystallised from water as needles, m. p. 260° (Found: C, 52·7; H, 5·35; N, 15·9. $C_8H_{10}ON_2S$ requires C, 52·75; H, 5·55; N, 15·4%); a further quantity of the substance (1·05 g.) separated from the pyridine solution after 2 days. It had $\lambda_{max.}$ 229 (ε 22,400), 263 mμ (ε 7900), $\lambda_{min.}$ 256 mμ (ε 7800) in water.

1-2′-Mercaptopropylthymine.—The foregoing pyrimidine (3·4 g.) was warmed with 2N-sodium hydroxide (25 ml.) for 20 min., a homogeneous solution being obtained. This was cooled and acidified with hydrochloric acid, yielding *1-2′-mercaptopropylthymine* (2·26 g.) which recrystallised from water as needles, m. p. 158° (Found: C, 47·8; H, 5·8; N, 13·9. $C_8H_{12}O_2N_2S$ requires C, 48·0; H, 6·05; N, 14·0%), $\lambda_{max.}$ 272 mμ (ε 10,350), $\lambda_{min.}$ 238 mμ (ε 2470) in water, giving a deep purple colour with alkaline sodium nitroprusside solution. The thiol (0·05 g.) in 0·1N-sodium hydroxide (5 ml.) was added to 0·1N-iodine in aqueous potassium iodide (2·5 ml.); the solution which was rapidly decolorised was acidified and the *disulphide* (0·042 g.) was collected and recrystallised from ethanol as prisms, m. p. 224° (Found: C, 48·4; H, 5·6; N, 13·8. $C_{16}H_{22}O_4N_4S_2$ requires C, 48·25; H, 5·55; N, 14·05%).

1-Propyl-2-thiothymine.—Propylamine (2·5 ml.) in ether (10 ml.) was added to β-methoxy-α-methylacryloyl *iso*thiocyanate (3·05 g.) in ether (10 ml.); a vigorous reaction occurred and *N-(β-methoxy-α-methylacryloyl)-N′-propylthiourea* separated. It crystallised from ethanol as needles, m. p. 56° (Found: C, 50·2; H, 7·35; N, 12·8. $C_9H_{16}O_2N_2S$ requires C, 50·0; H, 7·45;

N, 12·95%). The thiourea was heated on a water-bath with 2N-sodium hydroxide (10 ml.) for 5 min. The clear solution obtained was cooled and acidified, to give *1-propyl-2-thiothymine* (2·4 g.), needles (from ethanol), m. p. 200° (Found: C, 52·3; H, 6·45; N, 15·05. $C_8H_{12}ON_2S$ requires C, 52·15; H, 6·55; N, 15·2%).

1-Propylthymine.—A suspension of 1-propyl-2-thiothymine (0·5 g.) in water (30 ml.) and chloroacetic acid (0·6 g.) was boiled under reflux for 5 hr., then evaporated to an oil. This was evaporated twice with 10N-hydrochloric acid (2 ml.) and water (5 ml.), and the resulting residue dissolved in 5N-sodium hydroxide (4 ml.); the cooled filtered solution was acidified to give a crystalline precipitate. *1-Propylthymine* (0·4 g.) recrystallised from water as needles, m. p. 138° (Found: C, 57·15; H, 7·2; N, 16·4. $C_8H_{12}O_2N_2$ requires C, 57·15; H, 7·2; N, 16·65%). The compound had R_F 0·82 on paper chromatograms (ascending) in a solvent system composed of butanol saturated with water.

Reaction of 1-2′-Mercaptopropylthymine with Raney Nickel.—(*a*) The thiol (0·262 g.) in ethanol (40 ml.) and W2 Raney nickel (2 g.) were heated together under reflux for 2 hr.; tests of the solution with alkaline sodium nitroprusside then showed absence of thiol groups. The solution was evaporated and the solid crystallised from water, to give 1-propylthymine (0·05 g.), m. p. and mixed m. p. 138°, R_F 0·82 in butanol saturated with water. One other absorbing substance (R_F 0·48) was also present. (*b*) The thiol (0·25 g.) in ethanol (40 ml.) and W7 Raney nickel (2 g.) were heated together under reflux, and additional amounts of the catalyst (3 × 0·5 g.) were added at hourly intervals until a negative reaction for the thiol group with alkaline sodium nitroprusside was obtained (5 hr.). The catalyst was filtered off and washed with ethanol, and the filtrate evaporated to a solid residue. This was washed with water to give the disulphide (0·112 g.) which recrystallised from ethanol as prisms, m. p. and mixed m. p. 224°, R_F 0·7 in butanol–water. In a similar experiment, the thiol (0·25 g.), W7 Raney nickel (1 g.), and ethanol were boiled together for 4 hr., then kept overnight at room temperature to give the disulphide (0·13 g.). Neither 1-propylthymine nor the substance of R_F 0·48 (see *a*) could be detected on paper chromatograms.

5-Methyl-2-thio-5′-O-triphenylmethyluridine.—Recrystallised chlorotriphenylmethane (1·77 g.) was added to a solution of 5-methyl-2-thiouridine[3d] (0·87 g.) in pyridine (15 ml.), and the solution set aside for 2 days, then heated on a water-bath for 2 hr. The cooled solution was added to water (10 ml.) to precipitate a gum. The mixture was kept at 0° for 2 hr. and the aqueous phase decanted. The remaining semi-solid gum was washed by decantation with water, then stirred with acetone (16 ml.), to precipitate *5-methyl-2-thio-5′-O-triphenylmethyluridine* (0·87 g.) which recrystallised from ethanol as plates, m. p. 223° (Found: C, 67·3; H, 5·45; N, 5·5. $C_{29}H_{28}O_5N_2S$ requires C, 67·45; H, 5·45; N, 5·4%). A further quantity of the triphenylmethyl derivative (0·53 g.) was recovered by evaporation of the acetone filtrate and trituration of the residue with ether containing a little acetone; it had $\lambda_{max.}$ 277 mμ (ε 16,200), $\lambda_{min.}$ 247 mμ (ε 5000), in ethanol.

Reaction of 5-Methyl-2-thio-5′-O-triphenylmethyluridine with Methanesulphonyl Chloride.—Methanesulphonyl chloride (0·16 ml.) was added to a solution of the trityl derivative (0·97 g.) in pyridine (7 ml.), the mixture was set aside for 2 days, then evaporated to dryness *in vacuo*, and the residue rubbed with water (100 ml.) to give a solid (1 g.). This partly dissolved in benzene; the insoluble portion was collected and recrystallised from ethanol to give unchanged trityl derivative (0·21 g.), m. p. and mixed m. p. 223°. The benzene-soluble material was readily precipitated as a solid by addition of light petroleum (b. p. 40—60°). The solid, presumably a *hydrate* of *5-methyl-5′-O-triphenylmethyl-S*[1] : *2′-cyclothiouridine* (0·52 g.), was purified by several precipitations from benzene–light petroleum, then having m. p. 105° (to a glass) (Found: C, 66·5; H, 5·55; N, 5·4. $C_{29}H_{26}O_4N_2S,1\frac{1}{2}H_2O$ requires C, 66·4; H, 5·4; N, 5·35%), $\lambda_{max.}$ 270 mμ (ε 9050), $\lambda_{min.}$ 255 mμ (ε 7600), $\lambda_{infl.}$ 222 mμ (ε 26,450) in ethanol.

Thymidine.—The foregoing trityl compound (0·75 g.) in ethanol (100 ml.) and 0·1N-sulphuric acid (15 ml.) was heated on a water-bath for 2 hr. The solution was evaporated to a small volume *in vacuo* and water (25 ml.) added; triphenylmethanol (0·26 g.) was filtered off, and had m. p. and mixed m. p. 162—163°. The aqueous solution was just neutralised with "Deacidite FF," and evaporated *in vacuo* to a gum, $\lambda_{max.}$ 228 (ε 22,500), 266 mμ (ε 7850), $\lambda_{min.}$ 254 mμ (ε 7700) in water. A small amount of the gum was warmed for a few min. with 0·1N-sodium hydroxide; the solution then gave a purple colour with sodium nitroprusside and had $\lambda_{max.}$ 270 mμ and $\lambda_{min.}$ 240 mμ ($\varepsilon_{max.} : \varepsilon_{min.}$ 1·65). This gum (0·2 g.) in 0·1N-sodium hydroxide (10 ml.) was heated on a water-bath with W2 Raney nickel (1 g.) for 10 min.; the mixture was

XUM

filtered and the catalyst washed with water. The filtrate was just neutralised (to pH 7) with "Zeokarb 225." The solution then gave a deep blue colour with the Dische diphenylamine reagent, and paper chromatograms showed the presence of three spots which gave positive reactions with the cysteine spray reagent: R_F (butanol–water) 0·25, 0·36, 0·46 (butanol–acetic acid–water 5 : 2 : 3) 0·26, 0·45, 0·58. Thymidine had R_F 0·37 and 0·45 and 2-deoxyribose 0·25, 0·25 respectively in these solvent systems. The material of R_F 0·25 also gave positive tests for a reducing sugar with ammoniacal silver nitrate and aniline hydrogen phthalate. The above solution was evaporated *in vacuo* to a syrup which partly crystallised in 2 days. The solid was recovered after trituration with a little 80% aqueous ethanol and recrystallised from ethanol, to give thymidine (0·011 g.), m. p. and mixed m. p. 182—184° (Found: C, 49·8; H, 5·65; N, 11·95. Calc. for $C_{10}H_{14}O_5N_2$: C, 49·6; H, 5·85; N, 11·55%). The ultraviolet absorption spectra of the compound at different pH values were identical with those reported for thymidine in aqueous solution.[4]

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Sydney, N.S.W., Australia. [*Received, June 3rd,* 1958.]

[4] Fox and Shugar, *Biochim. Biophys. Acta*, 1952, **9**, 369.

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12. pseudo*Azulenes. Part II.** *A Tricyclic* cyclo*Penta*[b]-*thiapyran and Some Nitrogen Analogues.*

By G. V. Boyd.

The inherent instability of the indeno[1 : 2-*b*]pyran system has made possible the synthesis of the 2 : 4 : 5-triphenyl derivative of the new indeno-[1 : 2-*b*]thiapyran system, and of three substituted indeno[1 : 2-*b*]pyridines, from the corresponding pyrylium perchlorates. These *pseudo*azulenes * are green or blue bases; their solutions are susceptible to atmospheric oxidation. Their electronic absorption spectra are compared with that of the isosteric 1 : 2-benzazulene.

Derivatives of the *pseudo*azulenic * *N*-methyl*cyclo*penta[*b*]pyridine were first prepared by Armit and Robinson in 1922 and 1925. Condensing 6-aminopiperonaldehyde with 3-phenylindan-1-one, followed by quaternisation with methyl sulphate, yielded the salt (I; Y = $MeSO_4$), which on treatment with potassium hydroxide lost the elements of methyl hydrogen sulphate to form the green anhydro-base [1] (II). The structure of this compound is noteworthy because of the unfavourable *o*-quinonoid ring in its covalent canonical forms. Stabilisation is achieved by fusion to the aromatic *cyclo*pentapyridine system, together with the presence of the phenyl substituent, which seems important as attempts [2] to prepare the unsubstituted base (III) were inconclusive; a green amorphous solid was obtained, which decomposed in air and could not be purified.

It has now been found that the oxygen analogue, benzo[*b*]indeno[2 : 1-*e*]pyrylium tetrachloroferrate [3] (IV; Y = $FeCl_4$) does not yield the *pseudo*azulene (V) on treatment with base but affords 2-salicylideneindan-1-one (VI), a result not unexpected in view of a similar hydrolysis of 7 : 8-dimethoxybenzo[*b*]indeno[2 : 1-*e*]pyrylium chloride [3] (as IV).

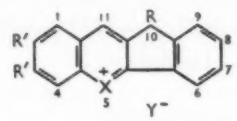
The 10-phenylbenzopyrylium salt (VII) was then examined in the hope that the phenyl substituent might stabilise the benzoindenopyran system. The perchlorate was prepared

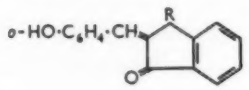
* Part I, *J.*, 1958, 1978. The term *pseudo*azulene is there explained as denoting a bicyclic compound with the π-electron structure of azulene, achieved by a skeleton other than that of fused C_5 and C_7 rings.

[1] Armit and Robinson, *J.*, 1925, **127**, 1604.
[2] *Idem*, *J.*, 1922, **121**, 827.
[3] Perkin, Robinson, and Turner, *J.*, 1908, **93**, 1085.

by acid-treatment of 3-phenyl-2-salicylideneindan-1-one (VIII), or, more efficiently, by condensing salicylaldehyde with 3-phenylindan-1-one in the presence of hydrogen chloride and perchloric acid.[4] The action of sodium hydroxide or sodium acetate on this salt again caused hydrolysis to the salicylidene compound rather than the formation of the anhydro-base (IX). This observation indicated that the oxygen analogues of azulene are less stabilised than the *N*-methyl analogues; and at the same time it opened a way into the field of the *N*-substituted *cyclo*penta[*b*]pyridines and of the hitherto unknown *cyclo*penta[*b*]thiapyrans.

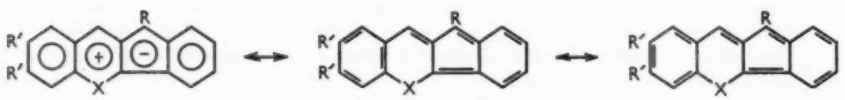
2 : 4 : 5-Triphenyl-5*H*-indeno[1 : 2-*b*]pyrylium tetrachloroferrate (X; Y = $FeCl_4$) was made by condensing 3-phenylindan-1-one with phenyl styryl ketone in the presence of ferric chloride and acetic anhydride, or, in much poorer yield, from 2-benzylidene-3-phenylindan-1-one and acetophenone. The corresponding perchlorate, like its 2 : 3-benzo-analogue, did not form an anhydro-base on treatment with alkali but suffered ring opening to the nearly colourless *pseudo*-base (XI). This is formulated as an αβ-unsaturated δ-diketone in accordance with Berson's recent spectroscopic work [5] on the *pesudo*-base of triphenylpyrylium. Structure (XI) represents a vinylogous β-diketone which accounts for the weakly acidic properties of the *pseudo*-base: it dissolves in alcoholic potassium hydroxide with a red colour, being reprecipitated on dilution with water. Treatment with acids regenerates the salts (X).



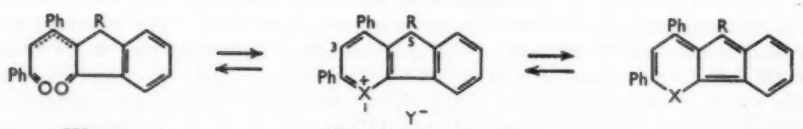


(I): X = NMe, R = Ph, R′R′ = OCH_2O
(IV): X = O, R = H, R′ = H
(VII): X = O, R = Ph, R′ = H

(VI): R = H
(VIII): R = Ph



(II): X = NMe, R = Ph, R′R′ = OCH_2O
(III): X = NMe, R = H, R′R′ = OCH_2O
(V): X = O, R = H, R′ = H
(IX): X = O, R = Ph, R′ = H



(XI): R = Ph

(XIX): R = H

(X): X = O, R = Ph
(XII): X = S, R = Ph
(XIV): X = NPh, R = Ph
(XVII): X = NMe, R = Ph
(XVIII): X = O, R = H
(XX): X = S, R = H

(XIII): X = S, R = Ph
(XV): X = NPh, R = Ph
(XVI): X = NMe, R = Ph

(XXI): X = NPh, R = H
(XXII): X = NMe, R = H

Formation of *pseudo*-bases is one example of the susceptibility of pyrylium salts to nucleophilic attack. The reaction with amines to yield pyridines has long been known; [6] recently Dimroth and his co-workers [7] obtained derivatives of nitrobenzene by reaction

[4] Cf. Le Fèvre, *J.*, 1933, 1532.
[5] Berson, *J. Amer. Chem. Soc.*, 1952, **74**, 358.
[6] Baeyer and Piccard, *Annalen*, 1911, **384**, 208.
[7] Dimroth *et al.*, *Angew. Chem.*, 1956, **68**, 519; *Chem. Ber.*, 1957, **90**, 1634, 1668.

with the potassium derivative of nitromethane, and Hafner [8] prepared azulenes by reaction with sodium *cyclo*pentadienylide. Pertinent to the present work is Wizinger's and Ulrich's synthesis [9] of thiapyrylium salts by the action of sodium sulphide on pyrylium salts, followed by acidification. Application of this elegant reaction to the pyrylium salt (X; Y = ClO_4) gave an excellent yield of the yellow 2 : 4 : 5-triphenyl-5*H*-indeno[1 : 2-*b*]-thiapyrylium perchlorate (XII; Y = ClO_4), which readily lost the elements of perchloric acid on treatment with sodium hydroxide, sodium acetate, or hot water, to yield the dark green *cyclo*penta[*b*]thiapyran (XIII).

This *pseudo*azulene, like the *cyclo*pentapyrans described in Part I, dissolves in acids to yellow solutions containing the cation (XII), and resists alkaline hydrolysis. It differs from them in its stability in boiling acetic acid, and in its sensitivity towards oxygen: the green colour of solutions in organic solvents, while stable for several hours in an atmosphere of nitrogen, fades within a few minutes on exposure to the air. The solid, however, has been kept unchanged in an open bottle for two weeks. Susceptibility to oxidation is also a property of the indenoquinoline (II) and is attributed to the presence of the quinonoid ring.

The action of aniline on 2 : 4 : 5-triphenyl-5*H*-indeno[1 : 2-*b*]pyrylium perchlorate led to the *N*-phenylpyridinium perchlorate (XIV; Y = ClO_4), which formed bluish-green 1 : 2 : 4 : 5-tetraphenylindeno[1 : 2-*b*]pyridine (XV) on decomposition with sodium hydroxide. Reaction of the pyrylium perchlorate with methylamine yielded the blue anhydro-base (XVI) directly, which was characterised as the pale yellow perchlorate (XVII; Y = ClO_4). Methylamine is thus a stronger base than the methylindenopyridine; the reverse relation holds with the *N*-phenyl compounds.

Attention was then turned to compounds lacking the 5-phenyl substituent. 2 : 4-Diphenyl-5*H*-indeno[1 : 2-*b*]pyrylium perchlorate (XVIII; Y = ClO_4) was prepared from indan-1-one and phenyl styryl ketone (31% yield) or from 2-benzylideneindan-1-one and acetophenone (9%). On hydrolysis with sodium acetate it gave the cream-coloured amphoteric *pseudo*-base (XIX) which was isolated in low yield after a troublesome purification. The derived thiapyrylium salt (XX; Y = ClO_4) decomposed on treatment with sodium hydroxide to an ill-defined yellow solid, which was not further examined. In the nitrogen series, however, the stable blue anhydro-base, 1 : 2 : 4-triphenylindeno-[1 : 2-*b*]pyridine (XXI), was readily obtained. The action of methylamine on the pyrylium perchlorate afforded a basic blue amorphous solid, probably impure 1-methyl-2 : 4-diphenylindeno[1 : 2-*b*]pyridine (XXII), which decomposed when kept and could not be purified.

The three indenopyridines closely resemble the sulphur compound: they are attacked by oxygen, resist the action of alkali and of acetic acid, and dissolve in acids to pale yellow solutions from which they are regenerated on basification.

In the presence of the unfavourable *o*-quinonoid ring, the diphenylindeno[1 : 2-*b*]-thiapyran system, unlike the *N*-phenyl and *N*-methyl analogues, thus requires the stabilising influence of a phenyl substituent in the five-membered ring for its formation (and, presumably, existence), while even this is not sufficient for the oxygen compound. Stabilisation of energetically unfavoured structures by aromatic groups is well known; *e.g.*, tetraphenyl*cyclo*pentadienone is stable but *cyclo*pentadienone itself seems incapable of any but the briefest existence.[10] The varying requirements for the 5-phenyl group, together with the lability of the *N*-methyl compound (XXII), suggest the following order of decreasing stability in the *pseudo*azulenes (XXIII): X = NPh > NMe > S > O. It is interesting that the resonance energies of the five-membered heterocyclic analogues of benzene are in the same sequence: 1-phenylpyrrole (76 kcal./mole) [11] > thiophen

[8] Hafner, *Angew. Chem.*, 1957, **69**, 393.
[9] Wizinger and Ulrich, *Helv. Chim. Acta*, 1956, **39**, 207.
[10] Deschamps, *Compt. rend.*, 1958, **246**, 3065.
[11] Schomaker and Pauling, *J. Amer. Chem. Soc.*, 1939, **61**, 1778.

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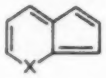
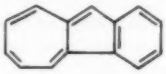
(27·7) [12] > furan (22·2).[12] The resonance energy of 1-methylpyrrole does not seem to have been recorded.

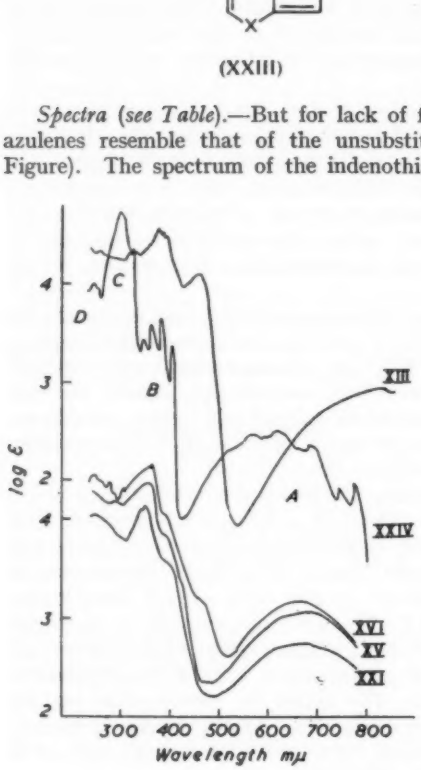


(XXIII)



(XXIV)

Spectra (*see Table*).—But for lack of fine structure, the spectra of the four *pseudo*-azulenes resemble that of the unsubstituted isosteric 1 : 2-benzazulene (XXIV) (see Figure). The spectrum of the indenothiapyran exhibits two intense absorption bands



Absorption spectra of 1 : 2-*benzazulene and the* pseudo*azulenes.*

The upper log ε scale refers to 1 : 2-benzazulene [13] (XXIV) and 2 : 4 : 5-triphenylindeno[1 : 2-*b*]-thiapyran (XIII). The lower scale refers to 1-methyl-2 : 4 : 5-triphenylindeno[1 : 2-*b*]pyridine (XVI). The curves for 1 : 2 : 4 : 5-tetraphenylindeno[1 : 2-*b*]pyridine (XV) and 1 : 2 : 4-triphenylindeno[1 : 2-*b*]pyridine (XXI) are displaced downwards by 0·2 and 0·4 unit in log ε, respectively.

Ultraviolet and visible spectra.

Compound †	Absorption max. (mμ) and log ε (in parentheses) D-Band	C-Band	B-Band	A-Band
1 : 2-Benzazulene [13] (XXIV) (in *cyclo*hexane)	222 (4·07) 248 (4·00)	298 (4·73) 307 (4·70) 321 (4·34)	346 (3·43) 363 (3·50) 383 (3·66) 404 (3·36)	565 (2·46) 615 (2·50) 682 (2·35) 742 (1·91) 776 (1·96)
2 : 4 : 5-Triphenylindeno[1 : 2-*b*]thiapyran (XIII)	260 (4·33) 320 (4·30) 324 (4·30) 327 (4·30)	380 (4·56) 385 (4·54) 389 (4·50) 392 (4·48)	460 (4·08)	825 (2·93)
1-Methyl-2 : 4 : 5-triphenylindeno[1 : 2-*b*]pyridine (XVI)	240 (4·45) 278 (4·37) 308 (4·30)	356 (4·55) 360 (4·55)	386* (4·05) 450* (3·21)	670 (3·16)
1 : 2 : 4 : 5-Tetraphenylindeno[1 : 2-*b*]-pyridine (XV)	294 (4·38)	356 (4·57)	390* (4·05)	685 (3·26)
1 : 2 : 4-Triphenylindeno[1 : 2-*b*]pyridine (XXI)	250 (4·45)	350 (4·53)	394* (3·96)	675 (3·15)

* Inflexion. † Solvent, dioxan, except where otherwise stated.

[12] Wheland, "Resonance in Organic Chemistry," Chapman and Hall Ltd., London, 1955, p. 99.
[13] Kloster-Jensen, Kováts, Eschenmoser, and Heilbronner, *Helv. Chim. Acta*, 1956, **39**, 1057.

centred at 385 and 460 mμ and a broad long-wave band, which correspond to the " C," " B," and " A " bands, respectively, of benzazulene.[13] The spectra of the nitrogen compounds are very similar; in every case the " B " band appears as a shoulder near 390 mμ; the spectrum of compound (XVI) has a second inflexion at 450 mμ.

The position of the absorption maxima in the visible spectra of substituted azulenes has been much discussed,[14] as charasteristic displacements are observed which depend on the position of the substituents. Introduction of a phenyl group into position 1 of azulene produces a bathochromic shift of 40 mμ [15] in the peak at the longest wavelength, compared with a bathochromic shift of only 10 mμ in passing from compound (XXI) to the analogously substituted phenyl derivative (XV). The weakness of the effect of the phenyl substituent in this case is ascribed to crowding: a molecular model shows that the 4- and the 5-phenyl group in the tetraphenylindenopyridine cannot both be co-planar with the ring system.[16]

Experimental

Operations with *pseudo*azulenes were carried out in an atmosphere of nitrogen. Absorption spectra were measured under nitrogen in dioxan containing a little quinol. Under these conditions the log ε values did not decrease by more than 0·01 unit during the determinations.

Hydrolysis of 10H-*Benzo*[b]*indeno*[2 : 1-e]*pyrylium Tetrachloroferrate.*—A suspension of the tetrachloroferrate [3] (IV; Y = $FeCl_4$) (1·4 g.) in ethanol (20 ml.) was shaken with 10% aqueous sodium hydroxide (30 ml.) and filtered. Addition of dilute hydrochloric acid to the filtrate precipitated 2-salicylideneindan-1-one (VI) (0·7 g.), which, after recrystallisation from ethanol, had m. p. 206° (decomp.), undepressed on admixture with an authentic specimen.[17]

3-Phenyl-2-salicylideneindan-1-one (VIII).—A solution of 3-phenylindan-1-one (4 g.) and salicylaldehyde (4 g.) in warm ethanol (30 ml.) was treated with potassium hydroxide (5·4 g.) in water (5·5 ml.) and set aside for 4 days. Addition of dilute acetic acid precipitated the *salicylidene derivative* (5·36 g., 75%), yellow needles (from aqueous acetone), m. p. 196·5—197° (decomp.) (Found: C, 84·6; H, 5·0. $C_{22}H_{16}O_2$ requires C, 84·5; H, 5·2%).

*10-Phenyl-*10H-*benzo*[b]*indeno*[2 : 1-e]*pyrylium Perchlorate* (VII; Y = ClO_4).—(*a*) Concentrated hydrochloric acid (6 ml.) was slowly added to a refluxing solution of the above salicylidene compound (1·5 g.) in acetic acid (25 ml.) and heating was continued for 15 min. Adding 20% perchloric acid to the cooled solution precipitated the *pyrylium perchlorate* (1 g., 53%), orange plates, m. p. 239—240° (decomp.) (from acetic anhydride–acetic acid) (Found: C, 67·0; H, 3·4. $C_{22}H_{15}O_5Cl$ requires C, 66·9; H, 3·8%).

(*b*) A solution of 3-phenylindan-1-one (3·12 g.) and salicylaldehyde (1·83 g., 1 mol.) in ether (50 ml.) containing 72% perchloric acid (5 ml.) was saturated with dry hydrogen chloride at 0°. During 24 hr. at 0° the solution deposited the foregoing perchlorate (4 g., 67·5%), m. p. and mixed m. p. 237—239°.

Hydrolysis of the perchlorate with cold aqueous-alcoholic sodium hydroxide or with sodium acetate in hot dilute acetic acid regenerated 3-phenyl-2-salicylideneindan-1-one.

*2 : 4 : 5-Triphenyl-*5H-*indeno*[1 : 2-b]*pyrylium Salts* (X).—Anhydrous ferric chloride (45 g.) was slowly added to an ice-cold solution of 3-phenylindan-1-one (17·1 g.) and phenyl styryl ketone (17·1 g., 1 mol.) in ether (150 ml.) and acetic anhydride (30 ml.). The mixture was refluxed for 1·5 hr., left overnight, then diluted with acetic acid, and the red *tetrachloroferrate* (23·7 g., 48·6%) was filtered off and washed successively with acetic acid and ether. It separates from acetone–ether in deep yellow platelets, m. p. 246—247° (decomp.) (Found: C, 61·0; H, 3·9. $C_{30}H_{21}OCl_4Fe$ requires C, 60·5; H, 3·6%). This chloroferrate was obtained in 20% yield by a similar condensation of equimolecular (0·05M) amounts of 2-benzylidene-3-phenylindan-1-one [18] and acetophenone. A solution of the chloroferrate (18·6 g.) in warm acetone (550 ml.) on treatment with 72% perchloric acid (5 ml.) deposited the *perchlorate*, yellow needles, m. p. 269·5—270° (decomp.) (Found: C, 72·4; H, 4·3. $C_{30}H_{21}O_5Cl$ requires C, 72·5; H, 4·3%).

[14] Gordon, *Chem. Rev.*, 1952, **50**, 185.
[15] Plattner, Fürst, Gordon, and Zimmermann, *Helv. Chim. Acta*, 1950, **33**, 1910.
[16] For a related case see Los, Saxena, and Stafford, *Proc. Chem. Soc.*, 1957, 352.
[17] Perkin and Robinson, *J.*, 1907, **91**, 1087.
[18] Pfeiffer and de Waal, *Annalen*, 1935, **520**, 185.

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2-(3-*Oxo*-1 : 3-*diphenylprop*-1-*enyl*)- *or* 2-(3-*Oxo*-1 : 3-*diphenylpropylidene*)-3-*phenylindan*-1-*one* (XI).—A mixture of the foregoing perchlorate (1·5 g.) and sodium acetate (0·5 g.) was boiled for 3 min. with acetic acid (20 ml.) containing water (3 ml.). The resulting clear yellow solution was poured into water, whereupon the pseudo-*base* separated (1·22 g., 97·5%). It crystallises from ethanol–acetone in cream-coloured needles, m. p. 153—154° (decomp.) (Found: C, 87·1; H, 5·1. $C_{30}H_{22}O_2$ requires C, 86·9; H, 5·4%). It dissolves in 10% ethanolic potassium hydroxide to a red solution from which it is reprecipitated on dilution with water. The *pseudo*-base (20 mg.) in acetone (3 ml.) was treated with 72% perchloric acid (3 drops). The solution became orange with a green fluorescence; ether precipitated the pyrylium perchlorate (X; Y = ClO_4) (20 mg.), m. p. and mixed m. p. 269° (decomp.).

2 : 4 : 5-*Triphenyl*-5H-*indeno*[1 : 2-b]*thiapyrylium Perchlorate* (XII; Y = ClO_4).—A suspension of the foregoing pyrylium perchlorate (2·0 g.) in acetone (60 ml.) was shaken for 5 min. with 10% aqueous sodium sulphide (12 ml.). The clear bluish-red solution was treated with 20% perchloric acid (18 ml.). The *thiapyrylium perchlorate* crystallised in yellow needles (1·92 g., 93%), m. p. 246—247° (decomp.) (Found: C, 70·3; H, 4·2; S, 7·1. $C_{30}H_{21}O_4SCl$ requires C, 70·2; H, 4·1; S, 6·3%).

When a suspension of the thiapyrylium perchlorate (1·7 g.) in boiling ethanol (60 ml.) was treated with a solution of sodium hydroxide (0·8 g.), or of sodium acetate (0·8 g.), in water (2 ml.), 2 : 4 : 5-*triphenylindeno*[1 : 2-b]*thiapyran* (XIII) separated in dark-green prismatic needles (1·1 g., 80·5%), m. p. 177—178° (not raised by crystallisation from ethyl acetate) (Found: C, 87·0; H, 4·7; S, 7·7. $C_{30}H_{20}S$ requires C, 87·3; H, 4·9; S, 7·8%). Hot water alone also decomposed the perchlorate, but more slowly. Adding perchloric acid to the dark green solution of the thiapyran in chloroform changed the colour to yellow; ether then precipitated the thiapyrylium perchlorate, m. p. and mixed m. p. 246—247° (decomp.). Dilute solutions of the thiapyran in organic solvents lost their green colour in 1—20 min., depending on the concentration, on exposure to air; but they were stable for at least 24 hr. in an atmosphere of nitrogen. The thiapyran (100 mg.) was refluxed with 10% ethanolic potassium hydroxide (10 ml.) for 20 min. On cooling, it (90 mg.) was recovered. It (20 mg.) dissolved in acetic acid (5 ml.) to a yellow solution with a green fluorescence. The solution was refluxed for 10 min. and then poured into water; the thiapyran (19 mg.) was recovered.

1 : 2 : 4 : 5-*Tetraphenylindeno*[1 : 2-b]*pyridine* (XV).—A suspension of the pyrylium perchlorate (X; Y = ClO_4) (2·5 g.) in ethanol (50 ml.) was treated with aniline (2 ml.) and refluxed for 10 min. On cooling, the resulting solution deposited 1 : 2 : 4 : 5-*tetraphenyl*-5H-*indeno*-[1 : 2-b]*pyridinium perchlorate* (XIV; Y = ClO_4) (1·7 g., 59%), which separated from acetic acid in pale yellow prisms, m. p. 280—282° (decomp.) (Found: N, 2·4. $C_{36}H_{26}O_4NCl$ requires N, 2·45%). This salt, on decomposition with aqueous-alcoholic sodium hydroxide, afforded the bluish-green *anhydro-base* (86%), needles (from aqueous acetone), m. p. 257° (Found: C, 91·8; H, 5·4; N, 3·1. $C_{36}H_{25}N$ requires C, 91·7; H, 5·4; N, 3·0%).

1-*Methyl*-2 : 4 : 5-*triphenylindeno*[1 : 2-b]*pyridine* (XVI) was prepared in 55% yield by shaking the pyrylium perchlorate (X; Y = ClO_4) (1·5 g.) with ethanol (50 ml.) and 30% aqueous methylamine (6 ml.) for 30 min. The anhydro-base was filtered off, washed successively with water and ethanol, and recrystallised from aqueous acetone, dark-blue needles, m. p. 170—171° (Found: C, 91·0; H, 5·55; N, 3·1. $C_{31}H_{23}N$ requires C, 90·9; H, 5·5; N, 3·4%). The *perchlorate* separates from acetone–ether in pale yellow needles, m. p. 180—181·5° (decomp.) (Found: N, 2·45. $C_{31}H_{24}O_4NCl$ requires N, 2·75%). Sodium hydroxide regenerates the *pseudo*azulene from this salt.

2 : 4-*Diphenyl*-5H-*indeno*[1 : 2-b]*pyrylium Tetrachloroferrate* (XVIII; Y = $FeCl_4$), orange rhombs (from acetone), m. p. 254—256° (decomp.) (Found: C, 56·5; H, 3·5. $C_{24}H_{17}OCl_4Fe$ requires C, 55·7; H, 3·3%), was obtained in the usual way, but without heating, from indan-1-one and phenyl styryl ketone (31·4%) or from 2-benzylideneindan-1-one and acetophenone (9%). It was converted into the yellow *perchlorate*, m. p. 269—270 (decomp.) (Found: C, 68·3; H, 4·05. $C_{24}H_{17}O_5Cl$ requires C, 68·5; H, 4·1%). The perchlorate (2 g.) was suspended in acetone (40 ml.), and a solution of sodium acetate (1 g.) in water (3 ml.) added. After 10 min. the mixture was filtered and poured into water. The dark gummy precipitate was dissolved in cold acetone and reprecipitated by water. After many repetitions of this procedure the *pseudo*-base, 2-(3-*oxo*-1 : 2-*diphenylprop*-1-*enyl*)- or 2-(3-*oxo*-1 : 2-*diphenylpropylidene*)-*indan*-1-*one*, was obtained as cream-coloured prisms (25 mg.), m. p. 128—129° (decomp.) (Found: C, 84·7; H, 5·5. $C_{24}H_{18}O_2$ requires C, 85·1; H, 5·4%). It forms the perchlorate on treatment

with perchloric acid, and dissolves in ethanolic potassium hydroxide with a red colour, being reprecipitated on addition of water.

2 : 4-*Diphenyl*-5H-*indeno*[1 : 2-b]*thiapyrylium perchlorate* (XX; Y = ClO_4), yellow, m. p. 228—229° (decomp.) (Found: C, 66·0; H, 3·85. $C_{24}H_{17}O_4SCl$ requires C, 66·0; H, 3·9%), was prepared from the foregoing pyrylium perchlorate in 80% yield as described for the 5-phenyl compound. This thiapyrylium salt (0·5 g.) was boiled for 10 min. with sodium hydroxide (0·3 g.) in water (1 ml.) and ethanol (25 ml.). The mixture was filtered from unchanged perchlorate (0·13 g.) and diluted with water. A dark-yellow ill-defined solid was precipitated, which was not further examined.

1 : 2 : 4-*Triphenyl*-5H-*indeno*[1 : 2-b]*pyridinium perchlorate*, pale yellow needles (from ethanol), m. p. 151—153° (decomp.) (Found: N, 2·5. $C_{36}H_{22}O_4NCl$ requires N, 2·8%), and 1 : 2 : 4-*triphenylindeno*[1 : 2-b]*pyridine* (XXI), blue needles, m. p. 239—240° (Found: C, 90·7; H, 5·3; N, 3·6. $C_{30}H_{21}N$ requires C, 91·1; H, 5·4; N, 3·5%), were prepared in 89% and 83% yields, respectively, by the methods described for the 5-phenyl compounds.

The three nitrogen anhydro-bases behaved like the sulphur compound when heated with ethanolic potassium hydroxide or with acetic acid, except that sodium hydroxide solution had to be used to decompose the acetates.

Attempt to prepare 1-*Methyl*-2 : 4-*diphenylindeno*[1 : 2-b]*pyridine* (XXII).—Shaking a suspension of 2 : 4-diphenyl-5*H*-indeno[1 : 2-*b*]pyrylium perchlorate (3·3 g.) in ethanol (100 ml.) for 1 hr. with 30% aqueous methylamine (12 ml.) gave a solid which was washed with ethanol, dissolved in dilute hydrochloric acid, and reprecipitated on basification as a blue powder (0·75 g.), m. p. *ca.* 133° (decomp.) (Found: C, 83·3; H, 5·35; N, 3·35%). This substance did not recrystallise; it decomposed to a pale green solid in a vacuum-desiccator overnight. Adding perchloric acid to an acetone solution yielded a red gum.

The author thanks Dr. F. L. Allen for his encouragement, Dr. E. Heilbronner, Eidgenössische Technische Hochschule, Zürich, for details of the spectrum of 1 : 2-benzazulene, and Mr. A. W. Ellis, B.Sc., for making the light absorption cell.

West Ham College of Technology, London, E.15. [*Received, July 28th*, 1958.]

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13. *The Abnormal Hydrolysis of Methyl β-Methylthio- and β-Ethylthio-propionate.*

By Frederick Challenger and Harry D. Hollingworth.

Methyl β-methylthio- and β-ethylthio-propionate, on hydrolysis with 6N-hydrochloric acid, give bis-2-carboxyethyl sulphide $S(CH_2{\cdot}CH_2{\cdot}CO_2H)_2$ and dimethyl and diethyl sulphide respectively. It is significant that ethyl methyl sulphide is not formed in the second reaction. Co-ordination of a proton by the sulphur atom followed by formation of dimethyl-β-propiothetin is believed to be the first stage. Two possible courses are discussed for the later stages, and the possible significance of acrylic acid. Alkaline hydrolysis yields methane- and ethane-thiol. Dimethyl sulphide is also evolved during conversion of methionine into homocystine by sulphuric acid and in the similar reaction with *S*-methylcysteine.

Barger and Coyne [1] found that ethyl β-methylthiopropionate $Me{\cdot}S{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2Et$ is hydrolysed by boiling N-hydrochloric acid to the expected liquid β-methylthiopropionic acid, and Liu [2] confirmed this result. When, however, the methyl ester [3] is hydrolysed with boiling 6N-hydrochloric acid we find that the product is a white acidic solid, m. p. 129°, having the empirical formula, $C_6H_{10}O_4S$. This was identified as bis-2-carboxyethyl sulphide, $(CO_2H{\cdot}CH_2{\cdot}CH_2)_2S$, by conversion into the sulphone. A volatile compound evolved during the hydrolysis was identified as dimethyl sulphide by conversion into the

[1] Barger and Coyne, *Biochem. J.*, 1928, **22**, 1417.
[2] Liu, Thesis, Leeds, 1948.
[3] Hurd and Gershbein, *J. Amer. Chem. Soc.*, 1947, **69**, 2333.

XUM

mercurichloride and the sulphidimine; it was free from methanethiol, as shown by its inertness to aqueous mercuric cyanide. Traces of both products are in fact also produced from methyl 2-methylthiopropionate even on use of N-acid. A similar experiment with 6N-sulphuric acid gave the same products, but also traces of methanethiol detected as its mercury derivative.

As expected, β-methylthiopropionic acid behaved in the same way with 6N-hydrochloric acid. β-Mercaptopropionic, methylthioacetic, and ethylthioacetic acid were stable to the hot 6N-acid.

It seemed probable that the liberation of dimethyl sulphide might be due to the formation and subsequent decomposition of the chloride of the closely related compound dimethyl-β-propiothetin, $Cl^-\{Me_2S^+\cdot CH_2\cdot CH_2\cdot CO_2H$. This might arise by isomerisation of the methyl β-methylthiopropionate, thus:

$$(1)\ Me\cdot S\cdot CH_2\cdot CH_2\cdot CO_2Me \longrightarrow Me_2S^+\cdot CH_2\cdot CH_2\cdot CO_2^- \longrightarrow Me_2S + CH_2{:}CH\cdot CO_2H$$

Such a mechanism recalls the interconversion of trimethylacetobetaine (" betaine ") and methyl dimethylaminoacetate demonstrated by Willstätter:[4]

$$(2)\ Me_3N^+\cdot CH_2\cdot CO_2^- \rightleftharpoons Me_2N\cdot CH_2\cdot CO_2Me$$

Betaine, however, is an α-derivative and although it seems possible from Willstätter's experiments that a similar relation may exist between trimethyl-β-propiobetaine and the methyl ester of β-dimethylaminopropionic acid:

$$(3)\ Me_3N^+\cdot CH_2\cdot CH_2\cdot CO_2^- \rightleftharpoons Me_2N\cdot CH_2\cdot CH_2\cdot CO_2Me$$

the evidence for this is not so clear. Heating the β-betaine gives mainly acrylic acid and trimethylamine. We find, however, that reaction (1) of the Willstätter type is not involved in the " abnormal " hydrolysis of methyl β-methylthiopropionate with hot acid. Under similar conditions methyl β-ethylthiopropionate gives diethyl sulphide and bis-2-carboxyethyl sulphide, and not ethyl methyl sulphide which would be expected if the reaction proceeded by mechanism (1). Moreover, ethyl β-methylthiopropionate gives dimethyl sulphide, and not ethyl methyl sulphide, with hot 6N-hydrochloric acid.

It seems fairly certain that the " abnormal " reaction is brought about by the low pH (6N-acid). Presumably a proton is co-ordinated by the unshared electrons of the sulphur atom of the methylthiopropionic acid to form the complex ion $MeHS^+\cdot[CH_2]_2\cdot CO_2H$. Dr. A. T. Austin has suggested that this might then be converted into the corresponding thetin by a process in which the positive charge on the sulphur atom might attract the electrons of the methyl group so as to allow bimolecular nucleophilic attack by the sulphur atom of a second molecule of β-methylthiopropionic acid, giving a transition state leading to the formation of the thetin and β-mercaptopropionic acid:

$$\begin{array}{ll} \overset{+}{H}S\cdot CH_2\cdot CH_2\cdot CO_2H & HS\cdot CH_2\cdot CH_2\cdot CO_2H \\ \vdots & + \\ \dot{C}H_3 & \\ \vdots & \\ MeS\cdot CH_2\cdot CH_2\cdot CO_2H & Me_2\overset{+}{S}\cdot CH_2\cdot CH_2\cdot CO_2H \end{array}$$

Elimination of dimethyl sulphide from the thetin would leave the cation $^+CH_2\cdot CH_2\cdot CO_2H$ which by union with β-mercaptopropionic acid, followed by deprotonation, could give bis-2-carboxyethyl sulphide:

$$^+CH_2\cdot CH_2\cdot CO_2H + HS\cdot CH_2\cdot CH_2\cdot CO_2H \longrightarrow H^+ + S(CH_2\cdot CH_2\cdot CO_2H)_2$$

This mechanism is preferable to that according to which a positive methyl ion is detached from the positively charged complex $MeHS^+\cdot CH_2\cdot CH_2\cdot CO_2H$ and after " independent

[4] Willstätter, *Ber.*, 1902, **35**, 584; Willstätter and Kahn, *Ber.*, 1904, **37**, 401, 1853.

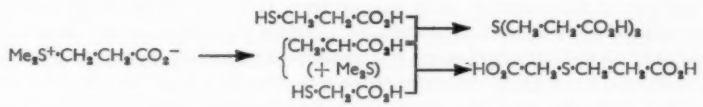
existence" is captured by a molecule of β-methylthiopropionic acid to give the thetin. Such a process, taking place in fairly strong hydrochloric acid, would be expected to give some methyl chloride. Attempts to detect this by passage of the volatile products from the abnormal hydrolysis of 10 g. of methyl β-methylthiopropionate through sulphuric acid to remove dimethyl sulphide and then through two traps at −20° and −75°, failed. Similar considerations arose in discussions of the mechanism of the mycological methylation of compounds of arsenic and selenium. If this involves a free methyl cation [5] the formation of methanol in aqueous cultures would be expected. Attempts by Mr. F. Kieffer at Leeds in 1945 to detect this failed.[6]

An alternative, though less concise, representation of the course of the abnormal hydrolysis involves decomposition of the thetin to dimethyl sulphide and acrylic acid as shown in (1) above.

By addition of the β-mercaptopropionic acid, produced by breakdown of the transition complex, to the acrylic acid, bis-2-carboxyethyl sulphide would be formed [7] and its production during the abnormal hydrolysis explained:

$$CH_2{:}CH{\cdot}CO_2H + HS{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2H = S(CH_2{\cdot}CH_2{\cdot}CO_2H)_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad (A)$$

It was found [8] that in hot 6N-hydrochloric acid β-mercaptopropionic acid reacts additively with methyl acrylate to form bis-2-carboxyethyl sulphide in good yield. A similar reaction with mercaptoacetic acid gives the unsymmetrical acid sulphide $CO_2H{\cdot}CH_2{\cdot}S{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2H$. Reaction (*A*) is therefore possible under the conditions of the abnormal hydrolysis. Moreover, by heating dimethyl-β-propiothetin bromide and 6N-hydrochloric acid with (*a*) β-mercaptopropionic acid and (*b*) mercaptoacetic acid the two acid sulphides were readily obtained:



When β-methylthiopropionic acid, mercaptoacetic acid, and 6N-hydrochloric acid were heated as before, both the symmetrical and the unsymmetrical acid were obtained. None of these experiments, however, enables a final decision to be reached as to whether acrylic acid is an intermediate in the original abnormal hydrolysis.

Formation of acrylic acid involves elimination of hydrogen from the β-position to the methylthio-group of the propiothetin. In αα-dimethyl-β-methylthiopropionic acid $MeS{\cdot}CH_2{\cdot}CMe_2{\cdot}CO_2H$ the β-hydrogens are replaced and this acid was recovered unchanged after long boiling with 6N-acid. Addition of thiols to unsaturated acids has usually been effected in neutral or mildly alkaline solution. Thus, Hurd and Gershbein [3] found that, in presence of sodium methoxide, methyl acrylate and thiophenol give methyl β-phenylthiopropionate. Our results described above and reported in a preliminary communication [8] show that this type of addition can occur in strongly acid solution. The same conclusion was reached almost simultaneously by Schöberl and Lange [9] who found that in 2N-sulphuric acid containing a trace of quinol, thioacetic and acrylic acid gave high yields of 2-carboxyethyl carboxymethyl sulphide. The formation of 1—5% of the isomeric acid $CO_2H{\cdot}CH_2{\cdot}S{\cdot}CHMe{\cdot}CO_2H$ was also detected by Kuhn–Roth oxidation. Schöberl and Lange found that when acids of the type $CO_2H{\cdot}CH_2{\cdot}CHR{\cdot}S{\cdot}[CH_2]_n{\cdot}CO_2H$ ($n = 1$ or 2) reacted with unsaturated acids, *e.g.*, $R{\cdot}CH{:}CH{\cdot}CO_2H$ in presence of saturated aqueous

[5] Challenger, *Quart. Rev.*, 1955, **9**, 268.
[6] Kieffer, unpublished observation.
[7] Holmberg, *Arkiv Kemi, Min., Geol.*, 1946, **21**, *B*, No. 7, 1.
[8] Challenger and Hollingworth, *Chem. and Ind.*, 1954, 463.
[9] Schöberl and Lange, *Annalen*, 1956, **599**, 140.

XUM

halogen acid, sulphonium salts $\{(CO_2H\cdot CH_2\cdot CHR)_2\cdot S^+\cdot[CH_2]_n\cdot CO_2H\}X^-$ were readily obtained. Many examples of this reaction were described. Such compounds may have been formed in our experiments with 6N-acid and have remained in the final mother-liquors. An attempt to detect β-mercaptopropionic acid when β-methylthiopropionic acid was boiled with 6N-acid and methyl α-methylacrylate failed, a viscous polymer and bis-2-carboxyethyl sulphide being obtained. The methyl derivative $CO_2H\cdot CH_2\cdot CH_2\cdot S\cdot CH_2\cdot CHMe\cdot CO_2H$ was not detected.

In hot aqueous 2N-sodium hydroxide methyl β-methylthiopropionate slowly afforded methanethiol, but not dimethyl sulphide, and after long boiling much of the acid was recovered. Acrylic acid could not be detected by addition of toluene-*p*-sulphinic acid and acidification. If formed it may have polymerised or undergone hydration to β-hydroxypropionic acid.[10] Methyl β-ethylthiopropionate gave ethanethiol on alkaline hydrolysis. Much unchanged acid was recovered. Formation of alkanethiol in these two reactions may arise by β-elimination or, less probably, by hydrolysis giving as second product acrylic acid or β-hydroxypropionic acid respectively.

In bread cultures of *Scopulariopsis brevicaulis* β-methylthiopropionic acid was shown by Challenger and Liu [11] to give methanethiol, some of which was methylated to dimethyl sulphide. Methylthio- and ethylthio-acetic acid gave no alkanethiol in cultures of *S. brevicaulis* which suggests that a β-elimination rather than hydrolysis of the C–S bond may be concerned in the case of β-methylthiopropionic acid.

The stability of methylthio- and ethylthio-acetic acid to 6N-acid (see above) is probably due to the proximity of the electrophilic carboxyl group to the sulphur atom. The unshared electrons of the sulphur are thereby rendered unavailable and co-ordination of a proton, the first step in the abnormal hydrolysis, is hindered. In the corresponding alkylthiopropionic acids or esters this effect is damped by the second intervening $-CH_2-$ group, and protonisation of the sulphur atom can occur. It appeared, however, of interest to see whether dimethylacetothetin chloride $Cl^-\{^+SMe_2\cdot CH_2\cdot CO_2H$, when heated with 6N-hydrochloric acid, would (the first stage of the series of reactions being by-passed) react in accordance with the later stages postulated for the course of the " abnormal " hydrolysis. This was found to be the case, the products being dimethyl sulphide, biscarboxymethyl sulphide, methylthioacetic acid, and trimethylsulphonium chloride. The last two were characterised as the *S*-benzylthiuronium salt and as the mercuri-iodide, respectively. Methylthioacetic acid is also produced when the thetin chloride is boiled under reflux with water or (personal communication from Dr. D. Leaver) with aqueous sodium hydroxide (glycollic acid is also formed in the latter case).

The decomposition of the acetothetin can be explained by an adaptation of the mechanism suggested above. (1) The thetin chloride breaks down into (*a*) methylthioacetic acid and methyl chloride, and (*b*) dimethyl sulphide and the ions Cl^- and $^+CH_2\cdot CO_2H$. The cation is then co-ordinated by methylthioacetic acid, giving the complex $HO_2C\cdot CH_2\cdot{}^+SMe\cdot CH_2\cdot CO_2H$. By reaction with the liberated dimethyl sulphide this complex might transfer its methyl group, probably without separation as an ion, giving trimethylsulphonium chloride and biscarboxymethyl sulphide. Since acrylic acid cannot be concerned in the decomposition of dimethylacetothetin chloride, the suggestion that it is not involved in the abnormal hydrolysis gains considerably in probability.

Decomposition of Methylthio-amino-acids by Hot Mineral Acid. S-*Methyl*-L-*cysteine*.—This was unchanged after long boiling with 6N-hydrochloric acid. Only traces of methanethiol were detected and no dimethyl sulphide. In boiling 18N-sulphuric acid, however, methanethiol, dimethyl sulphide, and dimethyl disulphide were evolved. The yield of dimethyl sulphide was much greater than that from methionine under similar conditions (see below), suggesting the greater instability of the thetin from *S*-methylcysteine than of that from methionine. An attempt to prepare the methiodide of *S*-methylcysteine by the method

[10] Linnemann, *Ber.*, 1875, **8**, 1095; Erlenmeyer, *Annalen*, 1878, **191**, 281.
[11] Challenger and Liu, *Rec. Trav. chim.*, 1950, **69**, 334.

XUM

employed for methionine methiodide,[12] reaction with methyl iodide in formic–acetic acid, yielded trimethylsulphonium iodide.

Methionine.—Butz and du Vigneaud [13] showed that in boiling 18N-sulphuric acid methionine gave homocystine and an odour resembling that of dimethyl disulphide. Repetition of this experiment and aspiration of the volatile products through mercuric cyanide and chloride showed the presence of methanethiol, dimethyl sulphide, and dimethyl disulphide. The monosulphide very probably arose by decomposition of the thetin $SO_4^{2-}\{[^+SMe_2 \cdot CH_2 \cdot CH_2 \cdot CH(NH_2) \cdot CO_2H]_2$, a reaction analogous to that observed in the abnormal hydrolyses reported above. In a comprehensive investigation Lavine *et al.*[14] showed that this thetin sulphate was formed during the action of sulphuric acid on methionine.

Experimental

Abnormal Hydrolysis of Methyl β-Methylthiopropionate.—The methyl ester [3] (2 g.) was heated under reflux with 6N-hydrochloric acid (10 c.c.) until the oil disappeared. The odour of a volatile compound of sulphur was noticed. The solution on extraction with ether yielded an oil, bis-2-carboxyethyl sulphide (1 c.c., crude oil), m. p. 130° (from water) alone or mixed with material prepared by Bennett's method [15] (Found: C, 40·2; H, 5·8; S, 17·7. Calc. for $C_6H_{10}O_4S$: C, 40·4; H, 5·65; S, 18·0%). It was converted by a slight excess of bromine water into bis-2-carboxyethyl sulphone, m. p. and mixed m. p. 219° (from water). Lovén [16] gives m. p. 210°. The authentic sample was, therefore, analysed (Found: C, 34·4; H, 4·6; S, 15·3. Calc. for $C_6H_{10}O_6S$: C, 34·3; H, 4·8; S, 15·3%).

Hydrolysis of methyl β-methylthiopropionate (1 g.) with 6N-hydrochloric acid (6 c.c.) was repeated and volatile products aspirated in a slow stream of nitrogen through water into (*a*) aqueous 4% mercuric cyanide to remove thiols and (*b*) aqueous 3% mercuric chloride to remove sulphides. After 30 min. a white solid was formed in (*b*) and the odour of sulphide in the wash-water was marked. After 8 hr. formation of solid ceased; when separated it had m. p. 157° and 156—157° in admixture with authentic dimethyl sulphide [17] mercurichloride of m. p. 157°. A trace of solid appeared in the mercuric cyanide which gave an odour of a thiol with hydrochloric acid, but was insufficient for determination of m. p. The dimethyl sulphide was further characterised by liberation from the mercurichloride with warm sodium hydroxide and aspiration into 10% aqueous chloramine-T. The resulting sulphidimine had m. p. 158° (from alcohol) and 157·5—158° with authentic *SS*-dimethyl-*N*-toluene-*p*-sulphonylsulphidimine.[18] Bis-2-carboxyethyl sulphide, m. p. 130°, was again obtained.

Similar results were obtained with 6N-sulphuric acid. Dimethyl sulphide was characterised as before. The trace of precipitate, m. p. 140°, in the mercuric cyanide evolved a thiol with hydrochloric acid.

Preparation of β-Methylthiopropionic Acid and its Decomposition with Hydrochloric Acid.—Methyl β-methylthiopropionate (20 g.) was completely hydrolysed (12 hr.) under reflux with N-hydrochloric acid (40 c.c.). A slight odour of dimethyl sulphide was noticed. Extraction with ether yielded the acid, b. p. 138—140°/25 mm. Barger and Coyne [1] give b. p. 235—240°/760 mm. A small amount of non-volatile oil (0·6 g.) solidified on cooling (m. p. 129°), and was doubtless bis-2-carboxyethyl sulphide, a small amount of which is evidently produced even when N-acid is used.

β-Methylthiopropionic acid with 6N-hydrochloric acid also gave dimethyl sulphide (characterised as before) and bis-2-carboxyethyl sulphide. Traces of methanethiol were recognised. Ethyl β-methylthiopropionate [19] when boiled with 6N-hydrochloric acid gave dimethyl sulphide

[12] Toennies and Kolb, *J. Amer. Chem. Soc.*, 1945, **67**, 849.
[13] Butz and du Vigneaud, *J. Biol. Chem.*, 1932—33, **99**, 135.
[14] Lavine and Floyd, *ibid.*, 1954, **207**, 97; Lavine, Floyd, and Cammaroti, *ibid.*, 1954, **207**, 107; Floyd and Lavine, *ibid.*, 1954, **207**, 119.
[15] Bennett, *J.*, 1927, 196.
[16] Lovén, *Ber.*, 1896, **29**, 1138.
[17] Challenger and Simpson, *J.*, 1948, 1591.
[18] Mann and Pope, *J.*, 1922, **121**, 1052.
[19] Haagen-Smit, Kirchner, Deasy, and Prater, *J. Amer. Chem. Soc.*, 1945, **67**, 1651.

XUM

(mercurichloride, m. p. 157°) as the only volatile sulphur compound; the solid product was bis-2-carboxyethyl sulphide.

β-Mercaptopropionic Acid and Hydrochloric Acid.—The mercapto-acid,[20] b. p. 127°/35 mm., evolved no hydrogen sulphide or alkyl sulphur compound when boiled with the 6N-acid for 9 hr. and 80% of the acid was recovered. A small amount of solid, m. p. 154°, was formed, presumably bis-2-carboxyethyl disulphide (m. p. 154°) produced by oxidation.

Methyl Methylthioacetate and Hydrochloric Acid.—The ester (0·5 g.) when heated under reflux with 6N-hydrochloric acid (4 c.c.) gave only traces of solid in the usual absorbents and the oil recovered by ether-extraction was insufficient for further work. Methylthioacetic acid, prepared by Ramberg's method,[21] had b. p. 111°/11·5 mm. (Holmberg [22] gives b. p. 106—108°/8 mm.) (Found: C, 34·5; H, 5·6; S, 29·9. Calc. for $C_3H_6O_2S$: C, 34·2; H, 5·7; S, 30·2%). The acid with boiling 6N-hydrochloric acid yielded no precipitates in the absorbents. Ether-extraction yielded the unchanged acid, characterised as the *S-benzylthiuronium salt*, m. p. and mixed m. p. 152° (from aqueous alcohol) (Found: C, 48·7; H, 6·0; N, 10·5; S, 23·9. $C_{11}H_{16}O_2N_2S_2$ requires C, 48·4; H, 5·9; N, 10·4; S, 23·5%). The stability to acid of methylthioacetic acid and its ester shown by these experiments was confirmed when the acid (1·0 g.), methyl acrylate (1·0 g.), and 6N-hydrochloric acid (6 c.c.) were heated under reflux for 8 hr. No odour, except that of the acid, was noticed and extraction with ether yielded the unchanged acid (1 c.c.), identified as the *S*-benzylthiuronium salt, m. p. 152°. Ethylthioacetic acid (1·0 g.) was also recovered unchanged from boiling 6N-hydrochloric acid, and no deposit appeared in the mercuric cyanide or chloride.

Preparation and Attempted Fission of αα-Dimethyl-β-methylthiopropionic Acid.—Chloropivalic acid [23] was esterified with methyl alcohol by Richard's method [24] for methyl pivalate. The *ester* had b. p. 162° (Found: C, 47·9; H, 7·4; Cl, 23·4. $C_6H_{11}O_2Cl$ requires C, 47·8; H, 7·4; Cl, 23·6%). Sodium thiomethoxide (0·1 mol.) and sodium chloropivalate in aqueous solution were warmed at 100° for 15 min.[21] The oil obtained on acidification was distilled at 30 mm., giving fractions, (*a*) b. p. 138—140° and (*b*) b. p. 155—160°. On redistillation, (*a*) boiled at 134°/12·5 mm. (Found: C, 48·8; H, 8·4; S, 21·0, 21·4. $C_6H_{12}O_2S$ requires C, 48·6; H, 8·2; S, 21·6%). Fraction (*b*) partially solidified, was free from sulphur, and may have contained some hydroxypivalic acid,[25] m. p. 124°. Hot 6N-hydrochloric acid and *methylthiopivalic acid* (*a*) gave no volatile products or odour of an alkyl sulphide or thiol. Ether extracted the unchanged acid. Its *S-benzylthiuronium salt* had m. p. and mixed m. p. 134° (decomp.) (from dioxan) (Found, for the authentic sample: C, 53·2; H, 7·4; N, 9·1; S, 20·2. $C_{14}H_{22}O_2N_2S_2$ requires C, 53·5; H, 7·1; N, 8·9; S, 20·4%).

Dimethyl-β-propiothetin Bromide and Hydrochloric Acid.—The bromide (1·0 g.) with hot 6N-acid (6 c.c.) quickly gave a strong odour of sulphide. A precipitate was formed in the mercuric chloride much faster than in the case of methyl β-methylthiopropionate. This had m. p. and mixed m. p. 157—158° with dimethyl sulphide mercurichloride. Methanethiol was absent. The reaction mixture yielded an oil containing halogen which partially solidified when rubbed with either 2-chloro- or 2-bromo-propionic acid: it was probably a mixture of the two.

Interaction of Dimethyl-β-propiothetin Bromide and Hydrochloric Acid in Presence of (a) *β-Mercaptopropionic Acid and* (b) *Mercaptoacetic Acid.*—(*a*) The bromide (1·0 g.) was boiled under reflux with β-mercaptopropionic acid (1·1 g.) and 6N-hydrochloric acid (6 c.c.) for 10 hr., until dimethyl sulphide ceased to be evolved. A solid was deposited overnight which when crystallised from water had m. p. and mixed m. p. 130° with bis-2-carboxyethyl sulphide. Bromine water gave bis-2-carboxyethyl sulphone (as before), m. p. and mixed m. p. 219°. (*b*) When mercaptoacetic acid (0·9 g.) was used instead of β-mercaptopropionic acid, extraction with ether yielded a white solid (1·4 g.), m. p. 86°. Crystallisation from benzene gave needles, m. p. 93° not depressing the m. p. (93·5°) of 2-carboxyethyl carboxymethyl sulphide.[16] This unsymmetrical acid is much more soluble than the symmetrical acid obtained as in (*a*) above.

Dimethylacetothetin and Hydrochloric Acid.—The thetin (1·0 g.) was boiled with 6N-acid (6 c.c.) for 9 hr. and volatile products were aspirated in nitrogen as before. There was no odour of methanethiol or deposit in the mercuric cyanide, but the mercurichloride of dimethyl sulphide

[20] Bülmann, *Annalen*, 1905, **339**, 363.
[21] Ramberg, *Ber.*, 1907, **40**, 2588.
[22] Holmberg, *Arkiv Kemi, Min., Geol.*, 1936, **12**, *A*, 11.
[23] Kharasch and Brown, *J. Amer. Chem. Soc.*, 1940, **62**, 925.
[24] Richard, *Ann. Chim. Phys.*, 1910, **21**, 335.
[25] Marcilly, *Bull. Soc. chim. France*, 1904, **31**, 119.

was obtained and converted into the sulphidimine, both of which were identified by m. p. and mixed m. p. The acid solution was evaporated in a vacuum to an oil which with alcohol–ether gave pale yellow needles, m. p. 140° (decomp.), presumably dimethylacetothetin chloride [m. p. 144° (decomp.)].

In a second experiment the acid solution when extracted with ether yielded a white semi-solid residue with an odour of methylthioacetic acid, which when crystallised from acetone–light petroleum formed needles, m. p. and mixed m. p. 130·5° with biscarboxymethyl sulphide (m. p. 130·5°) (Found: C, 32·0; H, 4·0; S, 21·3. Calc. for $C_4H_6O_4S$: C, 32·0; H, 4·2; S, 21·0%). The mother-liquor yielded methylthioacetic acid identified as the *S*-benzylthiuronium salt, m. p. and mixed m. p. 152°. Evaporation of the original aqueous solution gave a yellow oil which partially solidified in alcohol–ether and contained sulphur and halogen. With potassium mercuri-iodide it gave a white precipitate, m. p. 174—176°, which crystallised from acetone–ether in needles, m. p. and mixed m. p. 184° (decomp.) with authentic trimethylsulphonium mercuri-iodide $(Me_3S)_2HgI_4$, m. p. 184° (decomp.). The absence of an appreciable amount of biscarboxymethyl sulphide in the thetin anhydride was shown by dissolving 6 g. in dilute hydrochloric acid and extracting it six times with ether: this yielded a white solid with a sharp acidic odour in amount insufficient for a m. p. determination.

Attempts to detect Intermediate Products in the Reaction of β-Methylthiopropionic Acid and Hydrochloric Acid.—(a) *Acrylic acid.* β-Methylthiopropionic acid (5·6 g.), mercaptoacetic acid (3·0 g.), and 6N-hydrochloric acid (40 c.c.) were heated for 14 hr. (till the odour of dimethyl sulphide had disappeared). Extraction with ether yielded an oil which slowly crystallised. Since bis-2-carboxyethyl sulphide is almost insoluble in warm benzene and the unsymmetrical 2-carboxyethyl carboxymethyl sulphide is soluble, the white solid was crystallised from benzene but no homogeneous fraction could be obtained. Some fractions gave a negative test for the disulphide group with 10% aqueous sodium cyanide and sodium nitroprusside.[26] These were combined and crystallised from benzene–light petroleum, yielding fractions, (*a*) m. p. 129—130° not depressing that of authentic bis-2-carboxyethyl sulphide, and (*b*) m. p. and mixed m. p. 93—93·5° with 2-carboxyethyl carboxymethyl sulphide [Found for (*b*): C, 36·7; H, 4·4; S, 18·8. Calc. for $C_5H_8O_4S$: C, 36·6; H, 4·5; S, 19·8%. Calc. for $C_6H_{10}O_4S$: C, 40·4; H, 5·6; S, 18·0%]. Although the analysis for sulphur suggests that (*b*) contains 50% of bis-2-carboxyethyl sulphide the carbon and hydrogen figures do not confirm this. It is clear that the unsymmetrical acid arising from acrylic acid had been formed in large amount, a conclusion confirmed by the m. p. There was not sufficient material for a second determination of sulphur.

(b) *β-Mercaptopropionic acid.* 2-Methylthiopropionic acid (4·0 g.), methyl α-methylacrylate (1·8 g.), and 6N-hydrochloric acid (15 c.c.) were boiled in nitrogen for 14 hr. Much viscous polymer separated and the solution was extracted with ether, giving a white solid (2·0 g.) which yielded only bis-2-carboxyethyl sulphide, m. p. and mixed m. p. 130°. The unsymmetrical acid was not detected.

Methyl β-Ethylthiopropionate and Hydrochloric Acid.—The ester, prepared (yield 92%) from ethanethiol, methyl acrylate, and sodium methoxide by Hurd and Gershbein's method,[3] had b. p. 103°/35 mm. (Found: C, 48·7; H, 8·0; S, 21·5. Calc. for $C_6H_{12}O_2S$: C, 48·6; H, 8·2; S, 21·65%). This ester (2·0 g.) was heated with 6N-hydrochloric acid (10 c.c.) in nitrogen. Only traces of solid (giving an odour of a thiol with acid but insufficient for further work) appeared in a mercuric cyanide trap. The precipitate in the mercuric chloride trap, when crystallised from benzene, did not depress the m. p. (119°) of diethyl sulphide mercurichloride. Extraction of the acid with ether yielded an oil and traces of a solid, m. p. 127—128°, presumably impure bis-2-carboxyethyl sulphide. Oxidation of the oily mixture with ferric chloride gave white needles (from water), m. p. and mixed m. p. 219° with bis-2-carboxyethyl sulphone.

Methyl β-Phenylthiopropionate and Hydrochloric Acid.—When the ester[3] was boiled with hot 6N-hydrochloric acid no odour of a thiol or sulphide was noticed, no volatile products were detected, and β-phenylthiopropionic acid, m. p. 60·5°, was obtained in almost theoretical yield. Holmberg[27] gives m. p. 60—61°.

S-*Methylcysteine and Hydrochloric Acid.*—The amino-acid[28] had m. p. 242—244° (decomp.), $[\alpha]_D^{25}$ −32·4°. du Vigneaud *et al.*[28] give m. p. 245° and $[\alpha]_D^{27}$ −31·2°. The acid (0·5 g.) was

[26] Folin and Marenzi, *J. Biol. Chem.*, 1929, **83**, 103.
[27] Holmberg, *Arkiv Kemi, Min., Geol.*, 1942, **15**, *A*, 20.
[28] du Vigneaud, Loring, and Craft, *J. Biol. Chem.*, 1934, **105**, 481.

XUM

heated for 10 hr. under reflux with 6N-hydrochloric acid (5 c.c.). No volatile products were detected, the deposit in the mercuric cyanide being insufficient for a m. p. determination. The acid solution was poured into hot absolute alcohol (20 c.c.); *S*-methylcysteine, m. p. 240—242°, was precipitated with pyridine, a paper chromatogram, run in butanol–acetone and developed with ninhydrin, confirming its identity.

Attempted Preparation of S-*Methylcysteine Methiodide.*—Toennies and Kolb's method [18] for the corresponding methionine derivative was employed. *S*-Methylcysteine (2·7 g., 0·02 mole) in 89% formic acid (32·5 c.c.) was treated with glacial acetic acid (10 c.c.) and methyl iodide (5 c.c., 0·08 mole) and the closed flask kept at 25° in the dark for 7 days with occasional shaking, then evaporated under diminished pressure to a syrup. This when digested with methanol (20 c.c.) gave a yellow granular solid which was washed with methanol and acetone and precipitated from warm 50% ethanol with ether, forming needles, m. p. 202° (Found: I, 62·05; 61·95. Calc. for C_3H_9IS: I, 62·18%). Trimethylsulphonium iodide has m. p. 210°. The picrate, m. p. 180°, did not depress the m. p. of authentic trimethylsulphonium picrate, m. p. 180—181°.

Decomposition of DL-*Methionine with* 18N-*Sulphuric Acid.*—Methionine (5 g.) was boiled under reflux with 18N-sulphuric acid and the products aspirated as usual. Sulphur dioxide and dimethyl sulphide were detected by odour. Precipitates were formed in the mercuric chloride trap after 30 min. After 10 hr. sulphur dioxide was still present but the odour of dimethyl sulphide was not apparent. The precipitate in the cyanide trap had m. p. 150—155° (decomp.) and on crystallisation from ethyl acetate formed needles, m. p. and mixed m. p. 174° with mercury bisthiomethoxide. The original precipitate was greenish-yellow, probably owing to traces of the compound $(MeS)_2Hg,2HgS$.[29] The mercuric chloride precipitate (0·3 g.) sintered at 145—150° but did not melt below 200°. It was treated with sodium hydroxide and the volatile products were aspirated as usual. The mercuric chloride precipitate had m. p. and mixed m. p. 157° with dimethyl sulphide mercurichloride. The alkaline residue was then acidified. Aspiration into mercuric cyanide gave mercury bisthiomethoxide, m. p. and mixed m. p. 174° (from ethyl acetate). Clearly the volatile products from the reaction mixture contained dimethyl sulphide, methanethiol, and dimethyl disulphide.[29] Homocystine, m. p. 258—262° (decomp.), was isolated from the residual sulphuric acid according to Butz and du Vigneaud's directions.[13]

Decomposition of S-*Methylcysteine with* 18N-*Sulphuric Acid.*—*S*-Methylcysteine (1·0 g.) and 18N-acid (10 c.c.) were boiled under reflux and volatile products aspirated as usual. A deposit (A; 0·5 g.) was formed very quickly in the mercuric chloride and a smaller deposit (B) in the cyanide trap. (A) yielded dimethyl sulphide mercurichloride (C), m. p. and mixed m. p. 157°, on re-aspiration with sodium hydroxide into mercuric chloride. Subsequent acidification as before gave methanethiol, detected as the mercury derivative, $(MeS)_2Hg$, m. p. and mixed m. p. 174°. The yields of (A) and of (C) were much greater than in the corresponding experiment with methionine.

Addition of Mercapto-acids to αβ-*Unsaturated Acids in Hydrochloric Acid.*—(1) A mixture of β-mercaptopropionic acid (2 g., 0·02 mole) and methyl acrylate (1·6 g., 0·02 mole) was heated under reflux for 8 hr. with 6N-hydrochloric acid (10 c.c.). The oily layer soon disappeared. On cooling, much white solid was deposited which crystallised from water in needles (3·2 g., 91%), m. p. 130°, not depressing that of bis-2-carboxyethyl sulphide. The product was converted into the sulphone, m. p. and mixed m. p. 219°.

(2) 2-Carboxyethyl carboxymethyl sulphide was prepared by Lovén's method [16] by heating β-bromopropionic acid, mercaptoacetic acid, and aqueous sodium hydroxide under reflux for 30 min. and acidifying the mixture. It crystallised from benzene as plates, m. p. 93·5° (Lovén gives m. p. 94°) (Found: C, 36·8; H, 4·5; S, 19·6. Calc. for $C_5H_8O_4S$: C, 36·6; H, 4·5; S, 19·8%).

The same acid was obtained when mercaptoacetic acid (2·0 g., 0·025 mole) was heated under reflux with methyl acrylate (1·7 g., 0·025 mole) and 6N-hydrochloric acid (10 c.c.) for 10 hr. (until oil had disappeared and the liquid gave a negative test for the thiol group with nitroprusside). Extraction with ether yielded 3·2 g. (85%) of white solid, recrystallisation from benzene giving plates, m. p. 93° alone or in admixture with 2-carboxyethyl carboxymethyl sulphide.

(3) 2-*Carboxyethyl* 2-*carboxypropyl sulphide* was obtained when β-mercaptopropionic acid

[29] Challenger and Rawlings, *J.*, 1937, 868.

(2·0 g., 0·02 mole) was boiled with α-methyl methylacrylate (1·7 g., 0·02 mole) and 6N-hydrochloric acid (10 c.c.) for 8 hr. (until the clear solution gave a negative test for the thiol group). A viscous solid which appeared to be a polymer was deposited on cooling. The solution, after extraction with ether, yielded an oil, which solidified. Most solvents were unsuitable for recrystallisation, but 1 : 10 benzene–light petroleum yielded needles of the acid, m. p. 52·5° (Found: C, 43·5; H, 6·0; S, 16·7. $C_7H_{12}O_4S$ requires C, 43·7; H, 6·3; S, 16·7%).

Separation of $S(CH_2{\cdot}CH_2{\cdot}CO_2H)_2$ *from* $CO_2H{\cdot}CH_2{\cdot}CH_2{\cdot}S{\cdot}CH_2{\cdot}CHMe{\cdot}CO_2H$.—A mixture of 0·2 g. of each sulphide was prepared and fractionally crystallised from benzene. The more soluble, unsymmetrical, component was precipitated with light petroleum. Bis-2-carboxyethyl sulphide (m. p. 129—130°) and its 2-methyl derivative (m. p. 53°) were recovered.

Methyl Esters of β-Alkylthiopropionic Acids and Sodium Hydroxide.—Methyl β-methylthiopropionate (2·0 g.) was boiled with 2N-sodium hydroxide (10 c.c.) for 8 hr. and volatile matter was aspirated as before. Much deposit formed in the cyanide trap and crystallised from ethyl acetate, then having m. p. and mixed m. p. 175° with mercury bisthiomethoxide. In the mercuric chloride trap only traces of a solid were formed: this with dilute acid evolved methanethiol and was presumably $MeS{\cdot}HgCl,HgCl_2$ arising from fission of dimethyl disulphide formed by oxidation of the thiol in the air-stream.

Acidification of the alkaline reaction mixture and extraction with ether yielded an oil (1·5 g.) which solidified but readily melted in air. This, on evaporation with bromine water, gave β-methylsulphonylpropionic acid as needles, m. p. 105° (Schneider [30] gives m. p. 105°) (Found: C, 31·8; H, 5·2; S, 21·2. Calc. for $C_4H_8O_4S$: C, 31·6; H, 5·3; S, 21·1%).

In a similar experiment (3 hr.) an attempt to detect acrylic acid by addition of toluene-*p*-sulphinic acid to the alkaline solution and acidification failed, only the sulphinic acid, m. p. 85°, being precipitated. Both methyl acrylate and methyl α-methylacrylate were appreciably polymerised in boiling alkali under comparable conditions.

In a similar experiment with methyl β-ethylthiopropionate (2 g.) and 2N-sodium hydroxide (10 c.c.) (8 hr.) ethanethiol was collected as the mercaptide which, after crystallisation from ethanol, had m. p. and mixed m. p. 74°. Only traces of solid were formed in the mercuric chloride trap. Acidification of the alkaline reaction mixture yielded an oil which, with bromine water, gave β-ethylsulphonylpropionic acid, needles, m. p. 118° (from hot water) (Otto and Otto [31] give m. p. 112°) (Found: C, 36·5; H, 6·2; S, 19·6. Calc. for $C_5H_{10}O_4S$: C, 36·1; H, 6·1; S, 19·4%).

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[30] Schneider, *Annalen*, 1910, **375**, 233.
[31] Otto and Otto, *Ber.*, 1888, **21**, 992.

XUM

14. *An Examination of Some Approximations in Antisymmetrized Molecular-Orbital Calculations.*

By E. Theal Stewart.

A numerical study of some of the arbitrary simplifications adopted in " non-empirical " calculations on the energy levels of hydrocarbon π-electron systems indicates that (*a*) the customary approximations for three- and four-centre potential-energy integrals agree reasonably well *inter se*, and calculations on many-electron systems are thus probably not subject to significantly greater error than calculations on two-electron systems; (*b*) the analytical form of the carbon 2*s* wave function is not critical; (*c*) considerable uncertainty is introduced by the use of the W_{2p} *approximation*,

$$\int \phi_b(\mathrm{T} + \mathrm{V}_a)\phi_a \mathrm{d}\tau \sim W_{2p} \int \phi_b \phi_a \mathrm{d}\tau$$

Apart from the problems arising from the essential inflexibility of the molecular wave functions, Ψ, and the incompleteness of the Hamiltonian operator, H, " non-empirical " calculations on the energy levels of the π-electron systems of unsaturated or aromatic hydrocarbons are always beset by uncertainties resulting from the use of a number of arbitrary procedures (some inescapable) in the evaluation of the matrix elements $\int \Psi^* \mathrm{H} \Psi \mathrm{d}\tau$. In an attempt to assess the relative importance of the last source of error, a purely numerical study has been made of three possible difficulties: (*a*) recourse to approximate methods for evaluating three- and four-centre integrals; (*b*) the lack of any simple criterion for determining the optimum form of the carbon 2*s* wave function; (*c*) the adoption of the questionable W_{2p} approximation. Kinetic energies ($\mathscr{T}$), electron-repulsion energies ($\mathscr{U}$), and core-attraction energies ($\mathscr{V}$) have been considered separately; for purposes of illustration the antisymmetrized molecular-orbital (ASMO) calculations of Parr and Crawford [1] on ethylene and of Goeppert-Mayer and Sklar [2,3] on benzene have been chosen. No allowance has been made for configuration interaction or for σ–π exchange; and the original Goeppert-Mayer–Sklar technique [2] has been modified only in the ways indicated explicitly below.

The conventional value of 3·18 has been assigned to Z in the exponential factor, $\exp(-Zr/2)$, of the carbon 2*s* and 2*p* atomic wave functions. This value of the " effective nuclear charge " cannot be justified, and it is doubtless quite unsuitable in a molecular calculation; but there is at present no tolerably simple quantum-mechanical means of obtaining a better estimate. However, the Z-dependence of the results presented here has been tested (paper in preparation), and, except where the contrary is specified, it may be understood that the conclusions derived from an examination of Tables 1 and 2 hold good over a wide range of Z and R ($1 \leqslant ZR/2 \leqslant 6$), R being the C–C internuclear distance in Bohr radii.

Ethylene (*Table* 1).—Ethylene is the only molecule in which the electron-repulsion energy can be evaluated without resort to simplifications not fundamental to the Hückel π-electron approximation or the Goeppert-Mayer–Sklar procedure. It is thus most appropriate for an examination of Pariser and Parr's [4] " zero differential overlap " (z.d.o.) approximation, in which all integrals representing overlap between different atoms and all electron-repulsion integrals other than one- and two-centre Coulomb integrals are disregarded. It is clear from Table 1 that the enormous saving of computational effort which results (especially in more complex molecules) is fully justified. The maximum

[1] Parr and Crawford, *J. Chem. Phys.*, 1948, **16**, 526.
[2] Goeppert-Mayer and Sklar, *ibid.*, 1938, **6**, 645; Sklar and Lyddane, *ibid.*, 1939, **7**, 374; Parr and Crawford, *ibid.*, 1948, **16**, 1049.
[3] Stewart, *J.*, 1958, 4016.
[4] (*a*) Pariser and Parr, *J. Chem. Phys.*, 1953, **21**, 466, 767; (*b*) Parr and Pariser, *ibid.*, 1955, **23**, 711.

XUM

error of 0·35 ev found in ethylene is not large in relation to the standard of accuracy attainable in ASMO calculations of excitation energies. The very close approximation to the accurately computed electron-repulsion energy of the ground state [only] persists over a wide range of ZR, and is found also in the hydrogen molecule.

TABLE 1. *Ethylene: Composition of ground-state energy and excitation energies* (ev †)

Component ‡	2*s* orbital	^1A_g	$^1A_g - {}^1A_g{}^*$	$^1A_g - {}^1B_{1u}$	$^1A_g - {}^3B_{1u}$
$\mathscr{U}$ (accurate)	—	13·052	0·348	4·141	−4·204
$\mathscr{U}$ (z.d.o.)	—	13·083	0·000	3·852	−3·852
$\mathscr{T}$	—	58·480	28·542	14·271	14·271
$\mathscr{V}$	H-like	−99·981	−13·916	−6·958	−6·958
	nodeless	−96·460	−13·457	−6·729	−6·729
$\mathscr{T} + \mathscr{V}$	H-like	−41·501	14·626	7·313	7·313
	nodeless	−37·980	15·085	7·542	7·542
$\mathscr{W}$	H-like	−40·660	12·300	6·150	6·150
	nodeless	−36·722	11·609	5·805	5·805

C–C bond length = 1·353 Å (Gallaway and Barker, *J. Chem. Phys.*, 1942, **10**, 88).
^1A_g, $^1A_g{}^*$, $^1B_{1u}$, $^3B_{1u}$ correspond to Parr and Crawford's $^1\Psi_1$, Ψ_2, Ψ_V, Ψ_T.
†‡ See footnotes to Table 2.

While the use of approximation formulæ of the Mulliken type (see *Benzene* below) " almost with abandon " [4b] might perhaps be hazardous in some circumstances, it is easily shown that the zero differential overlap approximation is analytically equivalent ***in a two-electron system*** to an approximation in which Mulliken's formula for three- and four-centre integrals is extended to embrace *two*-centre exchange and ionic integrals.

In order to test the effects of a possibly poor choice of carbon 2s wave function, each of the present calculations has been carried out with the use of (i) a hydrogen-like wave function [5] and (ii) a function of the Slater type.[6] These presumably represent opposite extremes of unsuitability, (i) having a radial node much too far from the nucleus, (ii) having no radial node at all: it is thus noteworthy that the two sets of excitation energies differ by only ¼—½ ev for each electron excited. The agreement is at its worst at $Z \sim 3$. Inevitably, the ground-state " π "-electronic energy (which includes a substantial σ-π Coulomb contribution) is affected much more than the excitation energies.

It is conventional in ASMO calculations to *assume*, with Goeppert-Mayer and Sklar,[7] that there exists an eigenvalue W_{2p} such that

$$(\mathrm{T} + \mathrm{V}_a)\phi_a = W_{2p}\phi_a,$$

and hence

$$\int \phi_b(\mathrm{T} + \mathrm{V}_a)\phi_a \mathrm{d}\tau = \int \phi_b W_{2p}\phi_a \mathrm{d}\tau = \int \phi_b\phi_a \mathrm{d}\tau \,.\, W_{2p}$$

The functions ϕ_a and ϕ_b are carbon $2p$ wave functions, ***hydrogen-like*** in form, having their principal symmetry axes normal to the molecular plane, and their origins of co-ordinates at the nuclei of the carbon atoms a and b; T is the kinetic-energy operator; V_a represents the potential (as specified by Goeppert-Mayer and Sklar [2]) of the cationic core of the carbon atom a; and W_{2p} is a quasi-atomic parameter which I do not venture to define. (The number of non-equivalent definitions of W_{2p} is already almost equal to the number of published calculations embodying the W_{2p} approximation.) The term W_{2p} appears in the expression for the energy of each state of a homonuclear $2p\pi$-electron system with a coefficient equal to the number of π electrons, and it thus cancels out in the calculation of transition energies. [It does not follow (cf. Moser [7b]) that the *kinetic* energy is the same for all states.] A detailed appraisal of the W_{2p} approximation will be attempted in a later communication: it will suffice here to draw attention to the disturbingly large changes in calculated excitation energies which it brings about. While this major difficulty remains unresolved, it seems purposeless to introduce avoidable complexities into the original

[5] Kauzmann, " Quantum Chemistry," Academic Press Inc., New York, 1957, App. 3.
[6] *Idem*, ref. 5, Ch. 10.
[7] Goeppert-Mayer and Sklar, ref. 2; cf. (*a*) Ross, *Trans. Faraday Soc.*, 1952, **48**, 973; (*b*) Moser, *J. Chem. Phys.*, 1953, **21**, 2098.

XUM

Goeppert-Mayer–Sklar procedure (by taking account of configuration interaction, for example, or σ–π exchange).

Benzene (*Table* 2).—All the foregoing conclusions in respect of ethylene apply, ***mutatis mutandis***, to benzene; it is only necessary to consider the simplifications invariably adopted in the evaluation of three- and four-centre integrals. In four of the six transitions

TABLE 2. *Benzene: Composition of ground-state energy and excitation energies* (ev †).

(a) *Electron-repulsion energies* ($\mathscr{V}$)

Approximation for three- and four-centre integrals	$^1A_{1g}$	$^1A_{1g} - {}^1B_{1u}$	$^1A_{1g} - {}^1B_{2u}$	$^1A_{1g} - {}^1E_{1u}$	$^1A_{1g} - {}^3B_{1u}$	$^1A_{1g} - {}^3B_{2u}$	$^1A_{1g} - {}^3E_{1u}$
Mulliken	114·882	1·377	−0·024	4·193	−2·566	−0·134	−1·349
Sklar	113·633	1·901	0·521	4·401	−2·270	0·381	−0·944
z.d.o.	115·259	1·437	0·325	4·232	−2·089	0·325	−0·881

(b) *Kinetic energy and core-attraction energies*

Component ‡	2*s* orbital	Approximation for three-centre integrals	Ground-state energy	Excitation energy §
$\mathscr{T}$	—	—	172·333	13·212
$\mathscr{V}$	H-like	Mulliken	−452·511	−6·502
	H-like	Sklar	−450·977	−6·879
	nodeless	Mulliken	−441·302	−6·284
	nodeless	Sklar	−439·908	−6·630
$\mathscr{T} + \mathscr{V}$	H-like	Mulliken	−280·178	6·710
	H-like	Sklar	−278·644	6·333
	nodeless	Mulliken	−268·969	6·928
	nodeless	Sklar	−267·575	6·582
$\mathscr{W}$	H-like	Mulliken	−277·482	5·663
	H-like	Sklar	−275·962	5·285
	nodeless	Mulliken	−264·888	5·346
	nodeless	Sklar	−263·499	5·001

C–C bond length = 1·40 Å (Cox, *Rev. Mod. Physics*, 1958, **30**, 159).

A_{1g}, B_{1u}, B_{2u}, E_{1u} correspond to Stewart's $^3\Phi_0$, Φ_2, Φ_2, Φ_1 (or Φ_4).

† Fundamental constants are as given by Kauzmann (ref. 5, App. 1).

‡ $\mathscr{T}$ = kinetic energy; $\mathscr{W}$ = electron-repulsion energy; $\mathscr{V}$ = core-attraction energy; $\mathscr{W}$ = kinetic energy + core-attraction energy calculated with the use of the W_{2p} approximation (*i.e.*, $\mathscr{W} \sim \mathscr{T} + \mathscr{V}$).

$W_{2p} = -7{\cdot}889$ ev (H-like 2*s* orbital) or −6·199 ev (nodeless 2*s* orbital).

§ The six states considered differ only in electron-repulsion energy: all have the same kinetic energy and the same core-attraction energy.

represented in Table 2(*a*) the Mulliken [8] and the Sklar [9] approximations give electron-repulsion energies differing in opposite senses from those obtained with the use of the zero differential overlap approximation: this provides further justification for the use of Pariser and Parr's very simple procedure.

The Mulliken and the Sklar approximations to the electron-repulsion energies differ from each other by as much as 0·54 ev, but the difference is reduced significantly (to 0·17 ev or less) if the potential energies of attraction and repulsion are taken together:

	$^1A_{1g} - {}^1B_{1u}$	$^1A_{1g} - {}^1B_{2u}$	$^1A_{1g} - {}^1E_{1u}$	$^1A_{1g} - {}^3B_{1u}$	$^1A_{1g} - {}^3B_{2u}$	$^1A_{1g} - {}^3E_{1u}$
$\mathscr{W} + \mathscr{V}$ (Mulliken) ...	−5·125	−6·526	−2·309	−9·068	−6·636	−7·851
(Sklar)	−4·978	−6·358	−2·478	−9·149	−6·498	−7·823

[Hydrogen-like 2*s* orbital. Energies in ev.]

While only an exact evaluation of the three- and four-centre integrals can settle the question finally, it seems safe to suggest that, at least for $Z \sim 3$, the use of the Mulliken or Sklar approximation formulae does not lead to errors of consequence.

[8] Mulliken, *J. Chim. phys.*, 1949, **46**, 497; Rüdenberg, *J. Chem. Phys.*, 1951, **19**, 1433.
[9] Sklar, *ibid.*, 1939, **7**, 984; London, *ibid.*, 1945, **13**, 396.

XUM

The results of the present study do not support Moffitt and Scanlan's[10] view that (when the conventional value of the effective nuclear charge of carbon is used) ASMO calculations on benzene are subject to substantially greater uncertainty than those on ethylene.

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[10] Moffitt and Scanlan, *Proc. Roy. Soc.*, 1953, *A*, **220**, 530.

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15. *Triterpene Constituents of the Fruits of the Osage Orange* (Maclura pomifera).

By K. G. LEWIS.

The fruits of the osage orange have yielded butyrospermol and a new triterpene diol (probably lupane-3 : 20-diol) in addition to the lupeol reported previously.

LUPEOL was reported by Swift and Walter[1] and Beal and Wenzel[2] to be the only triterpene in the fruits of the osage orange (*Maclura pomifera*), but Wagner and Harris[3] later isolated a new substance which they called lurenol. The acetate of this substance was isolated from the crude material by acetylation and fractional crystallisation whereby lupenyl and lurenyl acetate were separated. On the basis of the properties of lurenol and its derivatives Wagner and Harris claimed that it was a new triterpene alcohol. They found[4] however, that when lurenol, obtained by hydrolysis of what they regarded as pure lurenyl acetate, was treated with benzoyl chloride and pyridine it yielded a product which was separable by fractional crystallisation into lupenyl benzoate and lurenyl benzoate. Further, when lurenol was re-acetylated by refluxing acetic anhydride and sodium acetate, lupenyl acetate and lurenyl acetate could be separated. Wagner and Harris claimed that lurenyl acetate was unaffected by the acetylating conditions used and they suggested that lurenol was related in structure to lupeol and that it could be converted into lupeol under acidic or basic conditions.

The crude material isolated by Wagner and Harris's procedure[3] was re-investigated in these laboratories, osage orange fruits * collected in the University grounds being used. The crude non-saponifiable material constituted about 5% of the dried fruit. Partial purification was effected by chromatography over alumina. The crystalline fractions eluted by light petroleum–benzene (fraction A) gave with the Liebermann–Burchard reagent a yellow colour, becoming brown with a strong green fluorescence, behaviour described by Wagner and Harris[5] as characteristic of lurenol. Further crystalline material (fraction B) was eluted by benzene–ether and this on purification afforded a product which gave a pale pink colour in the Liebermann–Burchard reaction and a negative test with tetranitromethane.

Fraction A was acetylated, affording lupenyl acetate and a more-soluble fraction, m. p. 144·5—147°. Hydrolysis of the latter acetate yielded the alcohol which was converted into the benzoate. The properties of these derivatives together with those recorded by

* Identified by the Botany Department of this University.

[1] Swift and Walter, *J. Amer. Chem. Soc.*, 1942, **64**, 2539.
[2] Beal and Wenzel, *Trans. Kansas Acad. Sci.*, 1951, **54**, 94 (*Chem. Abs.*, 1951, **45**, 5950).
[3] Wagner and Harris, *J. Amer. Pharm. Assoc.* (*Sci. edn.*), 1952, **41**, 494.
[4] *Idem, ibid.*, p. 497.
[5] *Idem, ibid.*, p. 500.

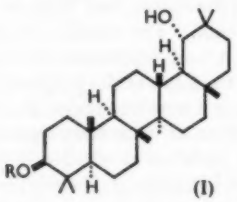
XUM

Wagner and Harris [3] for lurenol and by Heilbron, Jones, and Robins [6] for butyrospermol are compared in the Table.

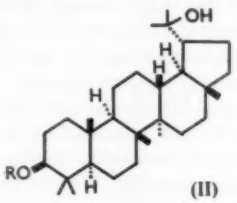
	Wagner & Harris		This work		Heilbron *et al.*	
	M. p.	$[\alpha]_D$	M. p.	$[\alpha]_D$	M. p.	$[\alpha]_D$
Alcohol	166—168°	+15·8°	111—112°	−13°	111—113°	−12°
Acetate	132—133·5	+19·9	144·5—147	+13	146·5—147·5	+11
Benzoate	125·5—126·5	+43·7	129—130	+33	130—133	+33·5

A mixed melting point of the alcohol obtained in this work with authentic butyrospermol showed no depression. It is possible that Wagner and Harris isolated a difficulty separable mixture of lupenyl and butyrospermyl acetate such as was encountered in working up the final mother-liquors from our acetate.

Fraction B melted over a rather wide range and was fractionally crystallised, to yield a product, m. p. 233—238°, unchanged on chromatography over alumina. This material gave an acetate which after chromatography had m. p. 248—250°. Analysis agreed with its formulation as a monoacetate of a diol $C_{30}H_{52}O_2$. It gave a negative tetranitromethane test and was transparent in the ultraviolet down to 212 mμ. It showed infrared bands at 3635 (non-bonded OH) and at 1738 cm.$^{-1}$ (CO of acetate) (in CCl_4). An unsuccessful attempt was made to form a diacetate and attempted oxidation with chromium trioxide–pyridine [7] yielded unchanged starting material. Dehydration by phosphorus oxychloride in pyridine gave in good yield lupenyl acetate.



(I)



(II)

This dehydration limits the possible structures for the parent diol (in the absence of other rearrangements) to 18α-oleanane-3β : 19α-diol (I; R = H) and lupane-3β : 20-diol (II; R = H). Ames, Davey, Halsall, and Jones [8] showed that the 19α-hydroxy-group of the monoacetate (I; R = Ac) was not acetylated under ordinary conditions and that this substance was dehydrated to form the lupeol-type of skeleton. It was however oxidizable to the 19-ketone. The evidence points to the structure of the diol monoacetate as (II; R = Ac) and experiments are in hand to confirm this.*

Experimental

M. p.s are corrected. Specific rotations were determined for chloroform solutions, ultraviolet absorption spectra for ethanol solutions with a Hilger Uvispek. Light petroleum refers to the fraction of b. p. 40—60°.

Extraction of the Fruit of Maclura pomifera.—Ripe fruit were sliced and oven-dried and then ground. The powdered material (250 g.) was extracted (Soxhlet) with light petroleum. Evaporation of the extract gave a brown oil (36 g.) which was refluxed in alcohol (1 l.) containing potassium hydroxide (40 g.) for 10 hr. Evaporation of most of the alcohol, followed by dilution with water and extraction of the solution with ether, yielded the non-saponifiable material

* At this stage of the work the Organic Chemistry laboratories of the University were destroyed by fire, so that proof of the structure has had to be deferred for some time.

[6] Heilbron, Jones, and Robins, *J.*, 1949, 444.
[7] Poos, Arth, Beyler, and Sarett, *J. Amer. Chem. Soc.*, 1953, **75**, 422.
[8] Ames, Davey, Halsall, and Jones, *J.*, 1952, 286.

(12·5 g., 5%) as a yellow oil which slowly solidified. This material (19 g.) was chromatographed in light petroleum–benzene (9 : 1) on alumina (B.D.H.). The material (11·5 g.) eluted by light petroleum–benzene was treated overnight with pyridine (25 ml.) and acetic anhydride (25 ml.). The mixture was filtered and the crystals (5·2 g.) were crystallised several times from methanol–chloroform, to yield lupenyl acetate, m. p. 218—219° (needles), $[\alpha]_D$ +42° (*c* 1·61) (Found: C, 82·1; H, 11·2. Calc. for $C_{32}H_{52}O_2$: C, 82·0; H, 11·2%). There was no m. p. depression on admixture with an authentic sample. Hydrolysis of this acetate yielded lupeol, m. p. 213—215° (mixed m. p. 213—215°) (Found: C, 84·6; H, 11·9. Calc. for $C_{30}H_{50}O$: C, 84·4; H, 11·8%), which yielded lupenyl benzoate, m. p. and mixed m. p. 268—270° (from methanol–chloroform), $[\alpha]_D$ +64° (*c* 1·35) (Found: C, 83·6; H, 10·4. Calc. for $C_{37}H_{54}O_2$: C, 83·7; H, 10·25%)

Isolation of Butyrospermyl Acetate.—The filtrate from the acetylation above was evaporated under reduced pressure and the residue was boiled with methanol and again evaporated. The solid residue, recrystallised from methanol–chloroform, had m. p. 129—135° (3·4 g.). After several recrystallisations this yielded butyrospermyl acetate, m. p. 144·5—147°, $[\alpha]_D$ +13° (*c* 0·88) (Found: C, 81·9; H, 11·0. Calc. for $C_{32}H_{52}O_2$: C, 82·0; H, 11·2%). The mother-liquors from the crystallisation of lupenyl acetate yielded an additional 460 mg. (total 2·06 g., *ca.* 0·5%). Hydrolysis of this acetate with potassium hydroxide in dioxan–methanol yielded butyrospermol, m. p. and mixed m. p. 111—112° (from aqueous methanol), $[\alpha]_D$ −13° (*c* 1·22) (Found: C, 84·6; H, 11·8. Calc. for $C_{30}H_{50}O$: C, 84·4; H, 11·8%), which with pyridine–benzoyl chloride gave the benzoate, m. p. 129—130° (from methanol–chloroform), $[\alpha]_D$ +33° (*c* 1·18) (Found: C, 83·7; H, 10·1. Calc. for $C_{37}H_{54}O_2$: C, 83·7; H, 10·25%).

Isolation of a New Diol.—The fraction of the non-saponifiable material eluted from alumina by benzene–ether (4 : 1) (fraction B) was rechromatographed. The material (3 g.), m. p. 220—230°, eluted by benzene–ether (9 : 1) was fractionally crystallised from methanol–acetone, to yield a product, m. p. 233—238°. The m. p. was unchanged on chromatography over neutral alumina (Woelm) and this material was treated with pyridine–acetic anhydride overnight. Working up of the reaction mixture yielded an acetate, m. p. 247—250° (from methanol–chloroform), which was chromatographed over neutral alumina (Woelm-Act I). Elution with benzene–ether (9 : 1) yielded the *diol monoacetate*, m. p. 248—250° (from methanol–chloroform), $[\alpha]_D$ +18° (*c* 1·22) (Found: C, 79·1; H, 11·4. $C_{32}H_{54}O_3$ requires C, 79·0; H, 11·2%).

Attempted formation of a diacetate. Heating the monoacetate (170 mg.) in pyridine (1 ml.) and acetic and anhydride (3 ml.) on a water-bath for 2½ hr. and recrystallisation of the product from methanol–chloroform yielded unchanged monoacetate, m. p. and mixed m. p. 247—250°.

Dehydration of the Diol Monoacetate.—The monoacetate (100 mg.) was refluxed in pyridine (15 ml.) and phosphorus oxychloride (3 ml.) for 2 hr. The cooled solution was poured on crushed ice, then extracted with benzene. The extracts were washed successively with dilute hydrochloric acid, dilute aqueous sodium hydroxide, and water. Evaporation yielded crystals which were chromatographed over neutral alumina (eluted by light petroleum), to give lupenyl acetate (85 mg.), m. p. and mixed m. p. 219—220° (from methanol–chloroform).

The author thanks Professor D. H. R. Barton, F.R.S., for samples of lupeol and its derivatives, and Professor E. R. H. Jones, F.R.S., and Dr. T. G. Halsall for the specimen of butyrospermol. The infrared spectrum was kindly determined by Dr. G. Eglinton of the University of Glasgow. The microanalyses were carried out by the C.S.I.R.O. Micro-analytical Laboratory under the direction of Dr. K. Zimmermann.

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XUM

16. *The Nitratonitrosylruthenium Complex*, $RuN_3O_{7\cdot5}$.

By F. S. Martin, J. M. Fletcher, P. G. M. Brown, and B. M. Gatehouse.

The ruthenium compound obtained by the reaction of nitric oxide with ruthenium tetroxide in carbon tetrachloride and referred to as $Ru_2N_6O_{15}$ by Martin and by Fletcher *et al.* has been further studied. Infrared examination has included the use of the ^{15}N form of the complex. The reactions involved in its preparation and its behaviour in both organic and aqueous media indicate that it may be a nitrato-complex containing two bisnitrosylruthenium groups linked by an oxo-bridge. Infrared absorptions of a number of other compounds containing the Ru–O bond are reported.

The ruthenium compound, originally formulated as $Ru_2N_6O_{15}$, was prepared by Martin [1] whilst endeavouring to obtain anhydrous, acid-free nitrosylruthenium nitrates. It was first suggested [2] that it is a binuclear oxygen-bridged nitrosylruthenium compound containing nitro-groups; the infrared spectrum (see below), however, shows the presence of nitrato- but of no nitro-groups. Then it was suggested [3] that each half of the molecule contains two bidentate nitrato-groups; however, reactions of its aqueous solutions more nearly correspond with the presence of one nitrato-group per atom of ruthenium. While there are good reasons for believing that each ruthenium atom in the complex is associated with at least one nitrosyl and one nitrato-group, the properties of the complex give no positive evidence about the arrangement of the third nitrogen atom: they indicate a structure of an unusual nature containing more than one ruthenium atom.

Experimental

Preparation and Stoicheiometry.—The compound $RuN_3O_{7\cdot5}$ was prepared as previously described,[1,2] by the action of dry nitric oxide on a dry solution of ruthenium tetroxide in carbon tetrachloride. Recent preparations confirmed the view that moisture, even in traces, leads to wide variations in composition, the ruthenium content varying from 32% to 39%, whereas rigorously dried reagents yield material constant in composition within narrow limits, and not differing significantly from our earlier preparations [1,2] [Found (three preparations): Ru, 38·6, 38·8, 38·5; N, 15·6, 15·9, 15·6. Calc. for $Ru_2O_{15}N_6$: Ru, 38·4; N, 15·9%].

It has been shown [1,2] that the preparative reaction employs a ratio of four mols. of nitric oxide to one of ruthenium tetroxide. In this experiment a known volume of dry nitric oxide was allowed to react with an excess of ruthenium tetroxide dissolved in carbon tetrachloride in a closed flask. When reaction was complete, the concomitant reduction in pressure enabled carbon tetrachloride to be admitted through a side tube. A volume corresponding to about seven-eighths of the original volume of nitric oxide entered. The residual gas was completely soluble in carbon tetrachloride since, after shaking of the flask, further ingress of carbon tetrachloride filled it.

Another experiment proved the gas to be very soluble in water. That it was nitrous oxide was confirmed by a mass spectrography, which disclosed also some nitrogen and traces of argon. Since the $^{40}A : N_2$ ratio in the sample ($^{40}A = 1{\cdot}22\%$ calc. on N_2) was almost identical with that in normal air (1·21%), the nitrogen in the sample was an atmospheric contamination. The only significant gaseous product is thus nitrous oxide. Any oxygen would of course have reacted to form nitrogen peroxide, which, incidentally, is not readily detected by mass spectrography.

This leads to the stoicheiometry: $8NO + 2RuO_4 = Ru_2N_6O_{15} + N_2O$.

Properties and Behaviour of the Complex.—The complex is pale orange-brown, diamagnetic ($\chi_g = -0{\cdot}08 \times 10^6$ at 21°), and very hygroscopic.

(*a*) Nitron acetate precipitates, from a cold, freshly prepared aqueous solution of the complex, a buff-coloured material containing most of the ruthenium. In a boiling mixture the

[1] Martin, Ph.D. Thesis, London, 1955.
[2] Fletcher, Jenkins, Lever, Martin, Powell, and Todd, *J. Inorg. Nuclear Chem.*, 1955, **1**, 378.
[3] Fletcher, Internat. Symp. on the Chemistry of the Coordination Compounds, Suppl. to *Ricerca sci.*, 1958.

XUM

buff precipitate decomposes, the ruthenium forms a pink solution (probably as a nitrosylruthenium acetate), and a precipitate of nitron nitrate is left. In 6 out of 10 experiments the number of nitrate groups found was one (and never less than one) per atom of ruthenium; in 4 out of 10 the number varied between 1·0 and 1·5.

(*b*) Ferrous solutions are quantitatively oxidised by nitrate in the presence of molybdate ions.[4] Since $RuNO^{III}$ does not normally oxidise ferrous ion, it should be possible to ascertain the number of nitrate groups in $RuN_3O_{7\cdot5}$ by its reaction with a ferrous solution. Aqueous solutions again showed a minimum of one nitrate group per ruthenium atom, (1·3—1·5 in 7 out of 10 cases).

(*c*) Water leads to the evolution of oxygen; the volume liberated varied from about 0·4 to 0·6 g.-atom of oxygen per g.-atom of ruthenium. Fresh aqueous solutions also decolorise permanganate. They are acidic and become more so on ageing or boiling. Plots of conductometric titrations with sodium hydroxide show well-defined but variable points of inflection (reminiscent of the neutralisation of a strong acid) which suggest an equivalent weight of about 400.

Although neither nitro- nor nitrito-groups are indicated by infrared examination (see below), nitrite is present in the supernatant liquid when alkaline solutions are boiled to precipitate nitrosylruthenium trihydroxide, $RuNO(OH)_3$ (cold alkalis do not give a precipitate). Thus, in an experiment in which the compound was dissolved in water, the reaction balance for oxygen, nitro-, and nitrate groups proved to be: O, 0·50; NO_2^-, 0·21; NO_3^-, 1·55. If the nitro-groups and the nitrate groups in excess of one arise through the oxidation of a nitrosyl group by oxygen in the molecule which is not associated with the nitrogen atoms, *e.g.*, by a reaction of the type, $[RuO_2(NO)_2NO_3]_2O + H_2O \longrightarrow 2RuNO^{3+} + xHNO_3 + yHNO_2 + zO_2$, the following relation should hold: (atoms of liberated oxygen) + (number of nitro-groups) + 2(number of nitrate groups minus one) = 2 for each ruthenium atom. The experimental figures cited give, per ruthenium atom, 0·5 + 0·21 + (2 × 0·55) = 1·81.

Passing hydrogen sulphide through hot aqueous solutions of the compound precipitates chocolate-brown nitrosylruthenium tri(hydrogen sulphide) [Found: Ru, 42·2; N, 6·0; S, 44·2. Calc. for $RuNO(SH)_3$ (cf. ref. 2): Ru, 43·9; N, 6·1; S, 42·7%]. The filtrate does not contain all the unprecipitated nitrogen; almost one nitrogen atom per ruthenium atom is lost from the hot system. Similar precipitation can be obtained from hot ethanolic solutions, and again nitrogen is lost.

(*d*) Most solvents containing oxygen (ethers, ketones, alcohols, esters) dissolve the solid compound readily. Its solubility in dioxan and acetophenone is low and it is insoluble in carbon tetrachloride, paraffins, benzene, etc. Boiling ethanol is oxidised rapidly to acetaldehyde; boiling acetone is slowly oxidised. Apparent molecular weights, determined ebullioscopically in the latter solvent, were over 500 ($Ru_2N_6O_{15}$ requires 526) and decreased slowly with continued boiling. In camphor (Rast's micro-method) the values were about 600 although some thermal decomposition occurred with the liberation of brown fumes. Cryoscopic observations in dioxan and acetophenone gave very variable values which decreased rapidly from about 327 to the anomalously low figure of 37: obviously there is extensive reaction with these and other solvents.

(*e*) Concentrated acids react with the solid. Cold sulphuric acid causes slight effervescence; with hot acid the colour changes to pinkish-brown, presumably by the formation of nitrosylruthenium sulphate, and thereby prevents the extraction of ruthenium into organic solvents. Cold hydrochloric acid slowly liberates brown fumes; the hot acid converts the compound rapidly into a raspberry-red solution of nitrosylruthenium chloride. Hot nitric acid yields a solution of nitrato-complexes of nitrosylruthenium; the reaction affords a convenient method of preparing these.[2]

Optical Examination.—(a) *Infrared spectra.* The infrared spectrum was examined in the region 2000—700 cm.$^{-1}$ and has been reproduced in ref. 3. The frequencies observed for this compound and for the compound containing ^{15}N (prepared by using NO enriched in ^{15}N) are listed in Table 1. The nitrosyl group gives rise to a very strong sharp peak at 1976 cm.$^{-1}$ (with ^{15}N the peak is observed at 1923 cm.$^{-1}$, the calculated shift being to 1921 cm.$^{-1}$); there is no splitting of this band. Bands at 1543 and 1276 cm.$^{-1}$ in the ^{14}N sample are assigned to ν_4 and ν_1 respectively [5] of the co-ordinated nitrato-group (–O·NO_2); the intensity of ν_1 is greater

[4] Kolthoff, Sandell, and Moskowitz, *J. Amer. Chem. Soc.*, 1933, **55**, 1454.
[5] Gatehouse, Livingstone, and Nyholm, *J.*, 1957, 4222.

XUM

than that of ν_4, but these intensities are usually comparable. They are shifted by 38 and 46 cm.$^{-1}$ respectively on ^{15}N substitution. Other bands arising from the co-ordinated nitrato-group occur at 847 (ν_6) and 788 cm.$^{-1}$ (ν_3 or ν_5).

Two broad bands at about 1160 and 970 cm.$^{-1}$ show insignificant shifts on ^{15}N substitution: the band centred at 970 cm.$^{-1}$ is not attributed to the ν_2 vibration of the nitrato-group (this vibration does not appear in other RuNO nitrato-complexes). Both bands may arise from vibrations of Ru–O bonds. The spectra of a number of other complexes, including those without nitrato-, nitro-, or nitrito-groups, containing ruthenium–oxygen bonds show similar broad

TABLE 1. *Infrared absorption bands (cm.$^{-1}$) for* $RuN_3O_{7\cdot5}$.

	100% ^{14}N	Approx. 73% ^{15}N	Approx. 81% ^{15}N		100% ^{14}N	Approx. 73% ^{15}N	Approx. 81% ^{15}N
^{14}NO	1976 vs, sp	1988 m, sh	1988 sh		~1160 m, b	~1152 m, vb	~1156 s, b
^{15}NO ...		1931 vs, sp	1923 vs, sp				1029 w
ν_2 H_2O? ...	1631 vw	1623 w	1639 w, sh		~970 s, vb	~956 m, b	~954 s, b
			1610 w, sh	ν_6 $O\cdot^{14}NO_2$	847 w	849 w, b	841 w
ν_4 $O\cdot^{14}NO_2$	1543 s	1513 s, sh	1502 sp, sh	ν_6 $O\cdot^{15}NO_2$ ...		817 w, b	822 w
$O\cdot^{15}NO_2$		1475 vs	1468 vs	ν_3 or ν_5	788 w	786 m, b	786 w
ν_1 $O\cdot^{14}NO_2$	1276 s	1305	1304 m, sh	ν_5 or ν_3 $O\cdot NO_2$	765 w	766 m, b	759 m, b
$O\cdot^{15}NO_2$		1259 s	1256 vs				

s = strong, vs = very strong, m = medium, w = weak, b = broad, vb = very broad, sp = sharp, sh = shoulder, vw = very weak.

The spectra were determined on a Grubb-Parsons double-beam infrared spectrometer equipped with an S3A monochromator and rock-salt optics. The samples were prepared as mulls in Nujol (2—15 μ) or hexachlorobutadiene (5—8 μ) in the regions of Nujol absorption. The rock-salt plates were coated with a fine film of polystyrene to prevent reaction with the compound.

bands between 900 and 1200 cm.$^{-1}$ (Table 2), and thereby support the hypothesis that this bond gives rise to frequencies in this region (cf. frequencies for other metal–oxygen bonds shown in Table 2).

TABLE 2.

Compound	Frequency (cm.$^{-1}$)		Compound	Frequency (cm.$^{-1}$)	Ref.
$[RuNO(NO_3)_3(H_2O)_2],2H_2O$	994 s, b		UO_2^{2+}	800—900 sym.	*a*
$Na_2[RuNO(NO_3)_4OH],2H_2O$	997 s	1170 vw		850—1000 asym.	
$[RuNO(NO_3)_3OH(H_2O)_2]$ ...	965 m	1151 m	OsO_4	935	
$RuNO(OH)_3$	939 w, vb	1098 m, b	$K[OsO_3N]$ ...	858, 890	*b*
RuO_2	1021 w	1094 w	$VOCl_3$	1035	*c*
$K_4[Ru_2Cl_{10}O]$	973 w	1153 w, 1164 w			

[a] Jones, *Spectrochim. Acta*, 1958, **10**, 395. [b] Lewis and Wilkinson, *J. Inorg. Nuclear Chem.*, 1958, **6**, 12. [c] Miller and Cousins, *J. Chem. Phys.*, 1957, **26**, 329.

A weak band at approximately 1630 cm.$^{-1}$ arises either as an overtone or combination band or from the bending vibration (ν_2) of the water molecule; if the latter, the amount of water present is very small.

(b) *Microscopic examination* (by E. WAIT). Use of polarised light revealed that the substance possessed no visible crystallinity and was not optically birefringent; hence it is either cubic in symmetry or, more probably, is amorphous. Studies by *X*-ray methods are therefore likely to be unrewarding.

DISCUSSION

The non-integral ratio of oxygen to ruthenium and the apparent molecular weight suggest that the compound is at least binuclear. An oxo-bridge between ruthenium atoms has been established for the ion $[Ru_2Cl_{10}O]^{4-}$ and there is evidence from other work in these laboratories that the linear oxygen-bridged group Ru–O–Ru is of wide occurrence: its existence in this complex would account for the observed diamagnetism (absence of unpaired electrons) even if the ruthenium is present as Ru(IV).

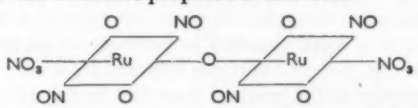
The consistent failure to find two nitrate groups per ruthenium atom excludes the composition $RuNO(NO_3)_2\cdot O\cdot RuNO(NO_3)_2$. A variant (suggested by Addison [6]) of this bidentate nitrate formulation is the bridging of two ruthenium atoms by such a group. Numerous structures with such bridging can be postulated for this complex, particularly

[6] Addison, Discussion in ref. 3.

if it is a polymer of relatively high molecular weight. Its existence as a polymer is consistent with its amorphous nature, which, however, is also characteristic of many non-polymeric compounds when prepared by precipitation.

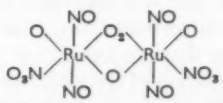
In the absence of evidence for such bridging, we suggest that the complex has two nitrosyl groups attached to each ruthenium atom, *i.e.*, is $RuO_2(NO)_2NO_3 \cdot O \cdot RuO_2(NO)_2NO_3$. Although there are very many nitrosylruthenium compounds [*i.e.*, containing the RuNO(III) radical], polynitrosylruthenium compounds are limited to the pentanitrosyl, $Ru(NO)_5$, and the complex, $RuO_4(NO)_2$ (prepared by an addition reaction between nitric oxide and ruthenium tetroxide [7]); the latter has a limited range of stability, is readily hydrolysed, and decomposes with loss of nitric oxide. Ruthenium's congener, iron, is also attached to two nitrosyl groups in certain nitrosyl halides, *e.g.*, $Fe(NO)_2I$, and Roussin's red salts, *e.g.*, $Fe(NO)_2SK$.

The observed properties of the complex in aqueous solution are consistent with our formulation: replacement of oxygen atoms by aquo-groups and the lability of the second nitrosyl group could lead to the liberation of oxygen, together with oxidation of the second NO group to mixtures of nitro- and nitrato-groups in proportions dependent on the conditions. The absence of splitting of the NO band observed in the infrared spectrum demands that two nitrosyl groups, if attached to one ruthenium atom, should be *trans* to one another (splittings up to 100 cm.$^{-1}$ have been observed for all compounds containing two or more *cis*-NO groups). Such a *trans*-dinitrosyl structure would be unstable, as is this complex even to the extent of smelling of oxides of nitrogen. The occurrence of the nitrosyl peak at a higher wave number than is usual for mononitrosyl ruthenium complexes (we have found values from 1840 to 1950 cm.$^{-1}$ in other RuNO complexes) is consistent with the strengthening of the N–O bond that would be expected if there are two *trans*-nitrosyl groups. By analogy with UO_2^{2+}, one would expect the (RuO_2) groups in our formulation to be linear: the structure proposed is therefore:



If each NO group carries a charge of +1 as in mononitrosylruthenium complexes, the ruthenium valency is IV.

To account for the release of oxygen, a structure with a single peroxo-bridge was also considered but rejected in terms of the overall properties. It has however been suggested by a Referee that a possible structure is:



One of the remarkable features of the reaction between nitric oxide and ruthenium tetroxide in carbon tetrachloride is the evolution of nitrous oxide. The significance of this may be to imply that the reaction is of a condensation type between unstable nitrosyl intermediates, *e.g.*:

$$-Ru\ldots.\boxed{ON + NO}\ldots.Ru- \longrightarrow (Ru{-}O{-}Ru) + N_2O$$

The reaction is quite different from that between liquid nitric oxide and ruthenium tetroxide at low temperatures.[7]

We are grateful to Messrs. E. R. Gardner, R. Todd, and J. Woodhead for experimental and analytical assistance, and to Professor R. S. Nyholm and Dr. J. Lewis for helpful discussions.

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UNIVERSITY COLLEGE, LONDON.

[*Received, August 6th*, 1958.]

[7] Hair and Robinson, personal communication.

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17. *Amino-acids and Peptides. Part II.* The Constitution of Hypoglycin A.*

By E. V. Ellington, C. H. Hassall, J. R. Plimmer, and C. E. Seaforth.

The structure (I) is proposed for the natural product hypoglycin A. This is based on spectroscopic evidence, examination of the products of catalytic hydrogenation, and identification of a product of acid-hydrolysis as 2-amino-5-methyl-4-oxohexanoic acid.

We were prompted to investigate the toxic constituents of the fruit of *Blighia sapida* (ackee) by a possible connexion between these fruits and Jamaican vomiting sickness.[1] Two compounds, hypoglycin A and hypoglycin B, were then isolated: they were so named because they had the unusual property of lowering the level of blood sugar when administered, orally or by injection, to rats and other test animals.[2] We have earlier given a brief account [3] of our results for hypoglycin A and proposed the structure α-amino-β-(2-methylene*cyclo*propyl)propionic acid (I). Descriptions of independent investigations in six other laboratories appeared at about the same time.[4] In what follows a detailed account is given of the evidence on which our proposal is based.

Paper-chromatographic and paper-electrophoretic results suggested that hypoglycin A was homogeneous, and countercurrent-distribution studies extending over 2000 transfers indicated a single impurity, in an amount less than 1%. Analysis of hypoglycin A and its (mono-)2 : 4-dinitrophenyl derivative indicated the formula $C_7H_{11}O_2N$. Hypoglycin A is optically active. There is a prominent band at 889 cm.$^{-1}$ in the infrared absorption spectrum, but the ultraviolet absorption spectrum, in both acid and alkali, shows end-absorption and closely resembles that of *iso*leucine. This indication of the unconjugated group $CH_2{=}C\lesssim$ was supported by the observation of Anderson *et al.*[4a,†] that 0·97 mol. of formaldehyde was released when hypoglycin A was oxidised by periodic acid. When hypoglycin A is hydrogenated in presence of platinum in acid conditions, there is a rapid uptake of one mol. of hydrogen followed by a very slow uptake of a second mol. Paper chromatography of the product from the first stage of the hydrogenation led to the separation of two ninhydrin-sensitive components. The major constituent, dihydrohypoglycin A, $C_7H_{13}O_2N$, was obtained by ion-exchange chromatography and showed no infrared band near 889 cm.$^{-1}$. The paper chromatogram of the product from the second stage of hydrogenation indicated a trace of material with the same R_F value as dihydroglycin A, but the major fraction was separated by ion-exchange chromatography into two isomers, $C_7H_{15}O_2N$. One of this pair was identified as 2-amino-5-methylhexanoic acid. The second was not identified with certainty but, since it differs from 2-aminoheptanoic acid, is probably a mixture of the diastereoisomers of 2-amino-4-methylhexanoic acid.‡

Evidence that led to the formulation of the structure of hypoglycin A was provided by acid-hydrolysis. Two-dimensional paper chromatography of the mixture obtained by use of hydrochloric acid showed the presence of at least twelve new ninhydrin-sensitive compounds: it was this result that led to the preliminary and incorrect opinion that hypoglycin A was a peptide.[2,5] A major constituent was distinguished by the yellow

* Part I, Hassall and Reyle, *Biochem. J.*, 1955, **60**, 334.

† We are grateful to Dr. Anderson and his co-workers for making this information available before its publication.

‡ Further evidence indicating such a mixture has been obtained recently.[4d]

[1] Hassall and Reyle, *West Indian Med. J.*, 1955, **4**, 83.

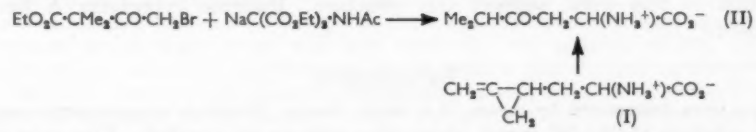
[2] Hassall, Reyle, and Feng, *Nature*, 1954, **173**, 356.

[3] Ellington, Hassall, and Plimmer, *Chem. and Ind.*, 1958, 329.

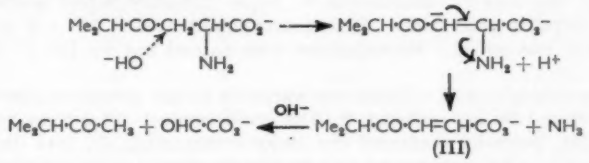
[4] (*a*) Anderson, Johnson, Nelson, Olson, Speeter, and Vavra, *ibid.*, p. 330; (*b*) Wilkinson, *ibid.*, p. 17; von Holt and Leppla, *Angew. Chem.*, 1958, **70**, 25; Renner, Jöhl, and Stoll, *Helv. Chim. Acta*, 1958, **41**, 589; (*c*) Carbon, Martin, and Swett, *J. Amer. Chem. Soc.*, 1958, **80**, 1002; (*d*) de Ropp, Van Meter, De Renzo, McKerns, Pidacks, Bell, Ullman, Safir, Fanshawe, and Davis, *ibid.*, p. 1004.

[5] von Holt and Leppla, *Bull. Soc. chim. belges*, 1956, **65**, 113.

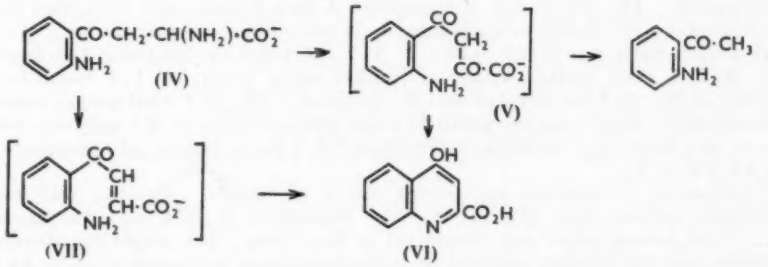
colour it gave with ninhydrin and has been identified as 2-amino-5-methyl-4-oxohexanoic acid (II). This constitution was suggested by hydrolysis with alkali to methyl *iso*propyl ketone and was confirmed by comparison with the amino-acid obtained when ethyl γ-bromo-αα-dimethyl-β-oxobutyrate was condensed with diethyl acetamidomalonate and then subjected to acid hydrolysis:



Hydrolysis of 2-amino-5-methyl-4-oxohexanoic acid with mild alkali (pH 8·5) liberates ammonia and affords 5-methyl-4-oxohex-2-enoic acid (III), whose structure is based on ultraviolet [6] and infrared spectra and conversion by concentrated alkali into methyl *iso*propyl ketone and glyoxylic acid:



These reactions are reminiscent of those suggested for the oxidation of kynurenine (IV) in alkaline conditions. In dilute alkali kynurenic acid (VI) is formed [7] but more concentrated alkali leads to *o*-aminoacetophenone.[8] The diketo-acid (V) has been proposed as an intermediate in both cases. As there is no direct evidence of the formation of compound



(V) we suggest, by analogy with the case of 2-amino-5-methyl-4-oxohexanoic acid, that the αβ-unsaturated acid (VII) is the intermediate in this degradation of kynurenine. There are good analogies for the cyclisation leading to a dihydroquinoline derivative,[9] for the oxidation of such a compound, by air, to kynurenic acid,[10] and, in triterpene chemistry [11] and elsewhere,[12] for the conversion of the αβ-unsaturated γ-keto-acids (III) and (VII) into methyl ketones during base-induced cleavage.

The formation of the keto-acid (II) on acid hydrolysis suggests that the terminal methylene group in hypoglycin A forms part of an allylic system which is associated with a ring structure. A van Slyke estimation on hypoglycin A indicates a free amino-group

[6] Raymond, *J. Amer. Chem. Soc.*, 1950, **72**, 4304.
[7] Butenandt, Weidel, Weichert, and von Derjugin, *Z. physiol. Chem.*, 1943, **279**, 27.
[8] Kotake and Kiyokawa, *ibid.*, 1931, **195**, 147; Kotake, *J. Chem. Soc. Japan*, 1940, **61**, 511.
[9] Fischer and Kuzel, *Ber.*, 1883, **16**, 163; Mannich and Dannehl, *Ber.*, 1938, **71**, 1899.
[10] Johnson and Buell, *J. Amer. Chem. Soc.*, 1952, **74**, 4517.
[11] Barton, de Mayo, and Orr, *J.*, 1958, 2240; Arigoni, Viterbo, Dünnenberger, Jeger, and Ruzicka, *Helv. Chim. Acta*, 1954, **37**, 2306.
[12] von Pechmann, *Ber.*, 1882, **15**, 891; Dixon, Gregory, and Wiggins, *J.*, 1949, 2139.

and the infrared absorption spectra of this compound and its reduction products contain maxima in the region of 3100, 1630, and 1510 (NH_3^+) and 1580 cm.$^{-1}$ (CO_2^-) which are characteristic of α-amino-acids. These observations, together with fission of the ring by hydrogenation to yield a mixture of α-amino-methylhexanoic acids, lead unambiguously to the structure (I) for hypoglycin A. The results reported by other laboratories, after completion of this work, support this structure. Racemic hypoglycin A has been synthesised.[4c]

Experimental

M. p.s were determined by means of a Kofler block. Rotation measurements employed aqueous solutions at 28—30° except where other solvents are specified. Ultraviolet spectra were determined on a Beckman spectrophotometer, model D.U. Infrared spectra were measured with potassium bromide discs unless otherwise stated. We are grateful to Dr. S. M. Nagy, Massachusetts Institute of Technology, and Dr. H. E. Hallam, University College, Swansea, for the determinations of infrared spectra. Amberlite ion-exchange resins were treated before use according to the makers' instructions.[13] Paper chromatography generally employed Whatman No. 1 paper in glass tanks. Papers were equilibrated at 30° ± 2° for 48 hr. before the eluting solvent was added. Microanalyses were carried out by Dr. F. Pascher, Bonn, Germany.

Purification of Hypoglycin A.—There was variation in the purity of different batches of hypoglycin A prepared by ion-exchange.[14] The crude product, after three recrystallisations from ethanol–water, generally contained one major contaminant, R_F 0·48 [butan-1-ol–acetic acid–water (4 : 1 : 5)]. Chromatography on a powdered cellulose column yielded hypoglycin A which was used for all subsequent investigations. This preparation has $[\alpha]_D^{26}$ +11° ± 1° (*c* 1·00), $[\alpha]_D^{26}$ +49·0° ± 1° (*c* 1·00 in water at pH 2) [Found: C, 59·2; H, 7·8; O, 22·8; N, 10·0; N (van Slyke), 10·7. Calc. for $C_7H_{11}O_2N$: C, 59·6; H, 7·9; O, 22·7; N, 9·9%], $\nu_{max.}$ 890 (>C=CH_2), 1760 (>C=CH_2 overtone), 1023 (*cyclo*propane-CH_2), 3100, 1630, 1510 (NH_3^+), and 1580 cm.$^{-1}$ (CO_2^-).

Homogeneity. The preparation of hypoglycin A gave a single spot when used for paper chromatography with the following solvents (R_F in parentheses; proportions are v/v): 1 : 1 : 1 Benzyl alcohol–water–butan-1-ol (0·29); 2 : 5 : 7 *tert.*-butyl alcohol–butan-1-ol–2N-ammonia (0·38); 2 : 2 : 1 ethyl methyl ketone–propan-2-ol–water (0·52); 4 : 1 : 5 butan-1-ol–acetic acid–water (0·59); 2 : 3 *tert.*-butyl alcohol–2N-ammonia (0·85); 3 : 2 ethyl acetate–water (0·90).

Hypoglycin A (42 μg.) was submitted to paper electrophoresis at 4·5 milliamp. and 90 v. It moved as a single spot on strips of Whatman No. 1 paper dipping into phosphate buffers at pH 4·0, 7·0, or 8·0.

Countercurrent distribution was carried out in an 80-tube apparatus, with *tert.*-butyl alcohol–ethyl acetate–water (25 : 50 : 52 v/v). Hypoglycin A (604 mg.) was dissolved in 40 c.c. of the bottom phase and distributed in four tubes. The weight-distribution curve determined after 150 transfers could not be distinguished from the theoretical curve for a single component. In an experiment involving 2000 transfers (kindly carried out on our behalf by members of the Research Division, The Upjohn Company, Kalamazoo, U.S.A.), comparison of the experimental and the theoretical curve indicated that the preparation of hypoglycin A was contaminated with less than 1% of an impurity that moved more slowly in this solvent system [*K* (hypoglycin A) 0·231].

N-2 : 4-*Dinitrophenylhypoglycin A.*—This was prepared in the usual way with 1-fluoro-2 : 4-dinitrobenzene. The product was amorphous even after purification by chromatography on columns of Celite or powdered cellulose. Paper chromatography [using *tert.*-butyl alcohol–phenol–phosphate buffer, pH 5·91 (1 : 1 : 1 v/v)] indicated that the main product (R_F 0·65) was contaminated with a trace of impurity (R_F 0·35). This preparation (1·40 g.) was distributed in 3 × 10 c.c. fractions in the lower phase of the system chloroform–methanol–0·1N-hydrochloric acid (2 : 2 : 1 v/v) and submitted to 585 transfers (with recycling) in an 80-tube countercurrent distribution apparatus. Measurement of optical density at 350 mμ and comparison with a theoretical distribution curve showed that the main fraction (*K* 0·059) was pure. This fraction was accumulated by evaporating the solvent from the appropriate tubes. The

[13] Bulletins No.'s M-3-47, IE-25-56, Rohm and Haas Coy., U.S.A.
[14] Hassall and Reyle, *Biochem. J.*, 1955, **60**, 334.

amorphous *product* was sublimed at 150—180°/0·2 mm. It has $\lambda_{max.}$ 360 mμ (ε 15,500) [Found: C, 51·3; H, 4·7; N, 13·0; O, 30·8%; *M* (Battersby and Craig [15]), 304. $C_{13}H_{13}O_6N_3$ requires C, 50·8; H, 4·3; N, 13·7; O, 31·2%; *M*, 307].

Hydrolysis of Hypoglycin A with Hydrochloric acid.—Hypoglycin A (10 mg.) was heated with 11N-hydrochloric acid at 150° in a sealed tube for periods varying from 3 to 148 hr. The residue obtained when the reaction mixture was filtered through Celite and evaporated to dryness was extracted with water. The solution was evaporated and the process was repeated until all traces of free hydrochloric acid were removed. The product, in 10% aqueous propan-2-ol (0·2 c.c.), was applied to Whatman No. 52 paper so that the spot contained 42 μg. of amino-nitrogen. Two-dimensional paper chromatography with butan-1-ol–acetic acid–water (4 : 1 : 5 v/v) in one direction and phenol–*m*-cresol–borate buffer (pH 9·3) in the other [16] led to an increasingly complex pattern of spots as the length of the degradation period increased up to 24 hr. Longer periods led to diminished intensity of some of the spots (see Table).

Two-dimensional paper chromatography of 24 hr. hydrolysis mixture.

R_F (phenol etc.)	R_F (butan-1-ol etc.)	Colour with ninhydrin	Intensity *	R_F (phenol etc.)	R_F (butan-1-ol etc.)	Colour with ninhydrin	Intensity *
0·03	0·16	Purple	3	0·72	0·59	Purple	1
0·05	0·22	Purple	4	0·73	0·35	Purple	5
0·16	0·16	Purple	3	0·70	0·47	Yellow	4
0·23	0·36	Purple	4	0·92	0·27	Brown-yellow	2
0·33	0·24	Purple	2				
0·65	0·29	Purple and yellow	4	0·93	0·33	Brown-yellow	2
0·72	0·45	Yellow	1				

* Decreasing intensity from 1 to 5.

Isolation of (−)-2-amino-5-methyl-4-oxohexanoic acid. Hypoglycin A (568 mg.) was hydrolysed under reflux with constant-boiling hydrochloric acid (50 c.c.) for 84 hr. The residue which remained after removal of the hydrochloric acid was dissolved in water (2 c.c.), filtered, and introduced on a column (75 × 2·7 cm.) of the ion-exchange resin Amberlite I.R.-4B (150—200 mesh). This resin had been washed successively with 0·1N-hydrochloric acid, excess of 0·2M-sodium acetate, and glass-distilled water. The column was eluted with distilled water (24 c.c./hr.); 10 c.c. fractions were collected and examined by paper chromatography. Fractions 23—40 (250 mg.) contained two compounds, R_F 0·38, 0·58 [butan-1-ol–acetic acid–water (4 : 1 : 5)] which gave yellow and purple colours, respectively, with ninhydrin. The individual components were obtained by paper chromatography of a band of the mixture on sheets of Whatman No. 52 paper. The *compound* with R_F 0·38 was eluted from the paper with water. Evaporation gave a residue which recrystallised from 92% ethanol as needles, m. p. 187—192°, $[\alpha]_D^{28}$ −5·9° ± 0·2° (*c* 2·7), $\lambda_{max.}$ 278 mμ (ε 32·5) in ethanolic 0·1N-hydrochloric acid [Found: C, 53·2; H, 8·5; N, 8·6; O, 30·2; N (van Slyke), 8·5%; *M* (Rast), 169. $C_7H_{13}O_3N$ requires C, 52·8; H, 8·2; N, 8·8; O, 30·2%; *M*, 159], $\nu_{max.}$ 1710 (CO), 3100, 1600, 1515, 1405 cm.$^{-1}$ (α-amino-acids).

Unlike the accompanying product the compound of m. p. 187—192° did not give a precipitate with Brady's reagent. When 15 mg. were heated in 1·5N-sodium hydroxide so that volatile material passed into aqueous 2 : 4-dinitrophenylhydrazine sulphate, methyl *iso*propyl ketone dinitrophenylhydrazone (12 mg.) was obtained (Found: C, 49·4; H, 5·4. Calc. for $C_{11}H_{14}O_4N_4$: C, 49·6; H, 5·3%), m. p. and mixed m. p. 119°. This and the authentic hydrazone gave identical infrared spectra.

(±)-*2-Amino-5-methyl-4-oxohexanoic Acid* (With Dr. R. F. Curtis).—*Ethyl γ-bromo-αα-dimethyl-β-oxobutyrate* was prepared by the procedure of Conrad [17] and Scheibler and Schmidt.[18] They did not record any constant. The product, n_D^{20} 1·4622, b. p. 119—122°/9 mm., decomposed when kept for several hours [Found: C, 39·2; H, 5·9; Br, 34·0; O, 20·6%; *M* (Rast), 230. $C_8H_{13}O_3Br$ requires C, 40·0; H, 5·5; Br, 33·8; O, 20·3%; *M*, 237].

Diethyl acetamidomalonate (5·8 g.) was dissolved in ethanolic sodium ethoxide (20 c.c.,

[15] Battersby and Craig, *J. Amer. Chem. Soc.*, 1952, **74**, 4023.
[16] Levy and Chung, *Analyt. Chem.*, 1953, **25**, 396.
[17] Conrad, *Ber.*, 1897, **30**, 857.
[18] Scheibler and Schmidt, *Ber.*, 1921, **54**, 144.

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from 0·6 g. of sodium) and kept at room temperature under anhydrous conditions for 16 hr. Ethanol was removed under reduced pressure. Ethyl γ-bromo-αα-dimethyl-β-oxobutyrate (6·2 g.) and dry benzene (45 c.c.) were added to the residue. After the mixture had been refluxed for 48 hr., sodium bromide was removed by filtration and the benzene was removed under reduced pressure, to give a red oil (9·2 g.). A portion of this red oil (7·33 g.) was subjected to short-path distillation. The forerun (2·8 g.) with b. p. up to 125°/0·9 mm. was rejected. *Triethyl 1-acetamido-4-methyl-4-oxopentane-1 : 1 : 4-tricarboxylate* was collected (2·15 g.); it had b. p. 125—130°/0·9 mm. and crystallised. Recrystallisation from ethyl acetate–light petroleum (b. p. 60—80°) gave prisms, m. p. 63—64° (Found: C, 55·2; H, 7·2; N, 3·7; O, 34·1; OEt, 33·5. $C_{17}H_{27}O_8N$ requires C, 54·7; H, 7·3; N, 3·8; O, 34·3; OEt, 36·2%).

A second portion of the red oil (1·03 g.) was kept at 80° for 16 hr. in concentrated hydrochloric acid (10 c.c.). A dark precipitate was removed. Evaporation of the filtrate gave a residue (0·35 g.), a sample (200 mg.) of which was placed on a column (56 × 1·7 cm.) of the ion-exchange resin Amberlite CG-45, Type I. The column was washed with glass-distilled water; 10 c.c. fractions of the eluate were collected. Glycine was eluted completely in fractions 8—20. *2-Amino-5-methyl-4-oxohexanoic acid* (115 mg.) was obtained pure from fractions 25—120. It crystallised from water–ethanol (4 : 1) as plates, m. p. 204° (decomp.) (Found: C, 52·9; H, 8·1; O, 30·3; N, 8·7%; *M*, 157. $C_7H_{13}O_3N$ requires C, 52·8; H, 8·2; O, 30·2; N, 8·8%; *M*, 159). The synthetic amino-acid and the natural optically active isomer gave identical R_F values in: butan-1-ol–acetic acid–water (4 : 1 : 5), R_F 0·39; acetone–water–butan-1-ol–pyridine (14 : 3 : 6 : 3), R_F 0·60; pyridine–methanol–water (10 : 77 : 20), R_F 0·20. However, these α-amino-acids gave a mixed m. p. 180° (decomp.). Their infrared absorption spectra showed minor differences.[19]

Racemisation of (−)-2-Amino-5-methyl-4-oxohexanoic Acid.—This was done by heating the optically active amino-acid (30 mg.) in glacial acetic acid (0·5 c.c.) with acetic anhydride (0·3 c.c.) for 1·5 hr. on a water-bath. Evaporation gave a viscous residue which was refluxed with 2·5N-hydrochloric acid (0·6 c.c.) for 1 hr. The residue obtained on evaporation was dissolved in water (3 c.c.) and purified by means of Amberlite CG-45, Type I. The resulting (±)-acid crystallised from water–ethanol (4 : 1) as plates, m. p. and mixed m. p. 204° (correct infrared spectrum).

Hydrolysis of (±)-2-Amino-5-methyl-4-oxohexanoic Acid with Sodium Hydrogen Carbonate.—(±)-2-Amino-5-methyl-4-oxohexanoic acid (140 mg.) and sodium hydrogen carbonate (360 mg.), dissolved in water (15 c.c.), were kept at 70—80° for 10 min. Ammonia was evolved. The solution was cooled and extracted with ether to remove any methyl *iso*propyl ketone. The aqueous layer was acidified with sulphuric acid and repeatedly extracted with ether. Evaporation of this extract gave white crystals (18 mg.) which sublimed as needles, m. p. 83°, $\lambda_{max.}$ 226 mμ (ε 15,000), $\lambda_{infl.}$ 320 mμ (ε 40) (Found: C, 58·8; H, 7·2; O, 33·9. $C_7H_{10}O_3$ requires C, 59·2; H, 7·0; O, 33·8%), $\nu_{max.}$ 1706 (CO_2^-), 1681 (conjugated C:O), and 1626 cm.$^{-1}$ (C=C). This product decolorised neutral permanganate at room temperature but gave no colour with ferric chloride solution. It was readily decomposed in excess of sodium hydroxide solution into methyl *iso*propyl ketone (2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 119°) and glyoxylic acid, which was identified by its reducing properties, by conversion into glycollic acid, and by its indole–sulphuric acid colour reaction.

These properties indicate that this product is *5-methyl-4-oxohex-2-enoic acid* (III).

Dihydrohypoglycin A.—Hydrogenation of hypoglycin A in glacial acetic acid in presence of platinum oxide led to an uptake of 1·05 mol. of hydrogen in 8 min. Paper chromatography of the product with butan-1-ol–acetic acid–water (4 : 1 : 5) showed the separation of two ninhydrin-sensitive spots, R_F 0·64 (major component) and 0·74. The mixture was applied to a column (24 × 1 cm.) of Amberlite CG-45, Type I. The column was eluted with water (10 c.c./hr.). Fractions (3 c.c.) were collected. Fractions 2—15 contained only the major component (R_F 0·64; 50 mg.). This, *dihydrohypoglycin A*, recrystallised from water–ethanol as plates, m. p. 201—209 (decomp.) (Found: C, 58·5; H, 8·9; O, 22·5; N, 9·8; *C*-Me, 10·9. $C_7H_{13}O_3N$ requires C, 58·7; H, 9·1; N, 9·8; O, 22·4; 1*C*-Me, 10·5%), $\nu_{max.}$ 1587 (CO_2^-), 1515, 3100 (NH_3^+), 2100 (methyl*cyclo*propyl-), 1020 cm.$^{-1}$ (*cyclo*propane-CH_2) and maxima characteristic of α-amino-acids. It was degraded with 10N-hydrochloric acid in a sealed tube at 100° for 6 hr., the reaction mixture being shown by two-dimensional paper chromatography (see above) to contain at least seven new ninhydrin-sensitive compounds.

[19] Brockmann and Musso, *Chem. Ber.*, 1956, **89**, 241.

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Tetrahydrohypoglycin A.—Dihydrohypoglycin A (250 mg.) in acetic acid (7 c.c.) containing 11N-hydrochloric acid (0·3 c.c.) was hydrogenated at 1 atm. in the presence of platinum oxide (184 mg.) for 30 hr. (uptake 0·95 mol.). Paper chromatography of the product distinguished two purple ninhydrin-sensitive spots, R_F 0·64 and 0·74 (major component) respectively. The hydrogenation mixture was applied to a column (29 × 1·7 cm.) of Amberlite resin CG-45, Type I. The column was eluted with water which was collected in 2 c.c. fractions. Fractions 110—260 gave the major component (126 mg.), (−)-2-*amino-5-methylhexanoic acid*, which gave a single spot on paper chromatography. It crystallised from water as plates, m. p. 220—225° (decomp.) (Found: C, 57·6; H, 10·1; O, 21·9; N, 9·4. $C_7H_{15}O_2N$ requires C, 57·9; H, 10·4; O, 22·0; N, 9·6%), $\nu_{max.}$ 3100, 1515 (NH_3^+), 1580 cm.$^{-1}$ (CO_2^-), and others characteristic of α-amino-acids.

The infrared absorption spectrum of racemised material was almost indistinguishable from that of a sample of (±)-2-*amino-5-methylhexanoic acid*, m. p. 215—225° (Found: C, 57·9; H, 10·4; N, 9·7%), prepared by the general procedure of Snyder, Shekleton, and Lewis.[20] Both these spectra differed markedly from that of (±)-2-aminoheptanoic acid,[21] m. p. 223° (decomp.), which was also prepared by the procedure of Snyder *et al.*[20] (Found: C, 57·8; H, 10·3; N, 9·6. Calc. for $C_7H_{15}O_2N$: C, 57·9; H, 10·4; N, 9·6%).

Ninhydrin degradation of the major component of tetrahydrohypoglycin A, by the procedure of Virtanen and Rautanen,[22] yielded a volatile aldehyde which was identified through the 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 91°, as *iso*hexanal. The infrared absorption spectra of the derivative, from the natural material and the authentic aldehyde were identical.

The minor component (Found: C, 57·8; H, 10·4; N, 9·7. Calc. for $C_7H_{15}O_2N$: C, 57·9; H, 10·4; N, 9·7%) from the hydrogenation mixture was racemised by acetic anhydride by the procedure outlined above. The infrared absorption spectrum differed markedly from that of (±)-2-aminoheptanoic acid and 2-amino-5-methylhexanoic acid. The minor component and the last-mentioned two amino-acids gave identical R_F values on paper chromatography in conventional solvent systems.

We are grateful for maintenance grants from the Government of Jamaica (to E. V. E.) and Eli Lilly and Co. (to J. R. P.). One of us (C. E. S.) is indebted to the University College of the West Indies for an Overseas Postgraduate Scholarship. We are indebted to members of the Research Division of the Upjohn Company, Kalamazoo, for making available unpublished information.

Department of Chemistry, University College of Swansea.
University College of the West Indies, Jamaica. [*Received, August 13th*, 1958.]

[20] Snyder, Shekleton, and Lewis, *J. Amer. Chem. Soc.*, 1945, **67**, 310.
[21] Helms, *Ber.*, 1875, **8**, 1167.
[22] Virtanen and Rautanen, *Biochem. J.*, 1947, **41**, 101.

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18. *Cardenolides. Part III.* The Constitution of Calotropagenin.*

By C. H. Hassall and (the late) K. Reyle.

Calactin is converted through calactinic acid into calotropagenin. On degradative evidence the aglycone is considered to be 3β : 12ξ : 14β-trihydroxy-19-oxo-5α-card-20(22)-enolide (II).

The shrub *Calotropia procera* (family Asclepiadaceae) occurs extensively in Asia and Africa. It has been used since antiquity as a galenical and for the preparation of arrow poison. Early attempts to isolate the biologically active constituents failed but pharmacological investigations showed that compounds with digitalis-like properties were present.[1,2] From the plant latex Hesse and his co-workers[2-4] separated calotropin ($C_{29}H_{40}O_9$),

* The communications in *J.*, 1951, 2766 and 3193, are regarded as Parts I and II, respectively.

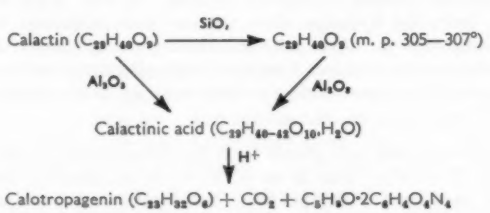
[1] Lewin, "Die Pfeilgifte," J. A. Barth, Berlin, 1923; Wehmer, "Die Pflanzenstoffe," Gustav Fischer, Jena, 1931, **2**, 1001.
[2] Hesse and Reicheneder, *Annalen*, 1936, **526**, 252.
[3] Hesse, Heuser, Hütz, and Reicheneder, *ibid.*, 1950, **566**, 130.
[4] Hesse and Lettenbauer, *Angew. Chem.*, 1957, **69**, 392.

XUM

calactin ($C_{29}H_{40}O_9$), uscharidin ($C_{29}H_{38}O_9$), uscharin ($C_{31}H_{41}O_8NS$), calotoxin ($C_{29}H_{40}O_{10}$), and voruscharin ($C_{33}H_{47}O_9NS$), and suggested that these were new steroid glycosides. The seeds of *Calotropis procera* were shown by Reichstein's school [5] to contain frugoside, coroglaucigenin, and corotoxigenin but very little, if any, of the crystalline steroids isolated from the latex.

In 1936, Hesse and Reicheneder [2] proposed the partial structure (I) for calotropin. A later investigation [3] provided evidence that the aglycone is common to the first five latex glycosides which are listed above. In a preliminary communication [6] we suggested structure (II) for this aglycone, calotropagenin. There has been independent support [7] for the proposal. Our detailed evidence is now presented.

The glycosides of *Calotropis procera* resist mild hydrolysis with dilute acid. It was this that prompted the unusual use of pyrolysis or hydrolysis with alkali for degradation.[2] However, these conditions led to decomposition of the aglycone. We have found that calotropagenin may be obtained easily from calactin. This is converted by alumina, either directly or through an isomer formed by the action of silica gel, into the new compound calactinic acid, $C_{29}H_{40-42}O_{10},H_2O$. This acid is hydrolysed readily by dilute sulphuric acid to calotropagenin, carbon dioxide, and a fragment which has been isolated as a bis-2 : 4-dinitrophenylhydrazone ($C_5H_8O{\cdot}2C_6H_4O_4N_4$). The calotropagenin which is prepared in this way is identical with the aglycone obtained in low yield from plant material.[2]



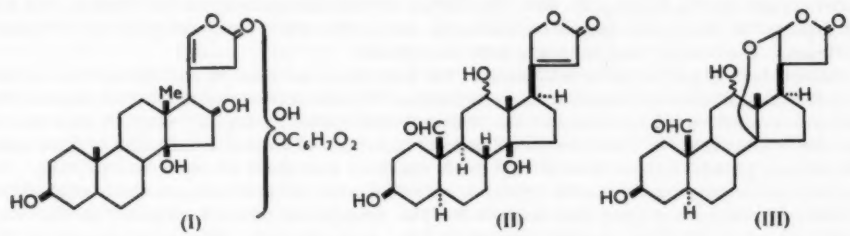
The ultraviolet and infrared absorption spectra of calotropagenin indicate that a but-20(22)-enolide ring is attached to the steroid portion. The maximum found at 310 mμ (log ε 1·4) is regularly observed in cardenolides with a 10-formyl substituent. This group also accounts for the reduction by sodium borohydride to a dihydrocalotropagenin which gives a positive Legal reaction, yields a triacetyl derivative, and is oxidised by chromic acid to a stable keto-acid, $C_{29}H_{28}O_7$.

The lactone ring, the 3 : 14-hydroxyl groups regularly found in cardenolides, and the 10-formyl group account for all but one of the oxygen atoms in calotropagenin. The last one is present in an acylatable hydroxyl group which is tentatively placed at position 12 to account for the formation of two *iso*-derivatives when calotropagenin reacts with mild alkali. One of these (III) evidently results from the well-known interaction of the αβ-unsaturated lactone with the hydroxyl group at position 14. The second could be formed by interaction with a hydroxyl group at positions 12, 15, or 16. Position 15 is unlikely as calotropagenin is not oxidised by periodic acid during 56 hours; and position 16 is excluded since vigorous treatment with hydrochloric acid does not lead, as in the case of gitoxigenin, to a $\Delta^{14:16}$-dianhydro-derivative with an absorption maximum near 337 mμ.[8]

The stereochemistry of calotropagenin is suggested by analogy with other cardiac glycosides obtained from Asclepiadaceae. In particular, attention has been drawn to the fact that cardenolides isolated from species of this plant family have *trans*-A/B rings.

[5] Rajagopalan, Tamm, and Reichstein, *Helv. Chim. Acta*, 1955, **38**, 1809.
[6] Hassall and Reyle, *Chem. and Ind.*, 1956, 487.
[7] Geiger, Hesse, Lettenbauer, and Schildknecht, *Naturwiss.*, 1957, **44**, 328.
[8] Tschesche, *Chem. Ber.*, 1937, **70**, 1554.

There is evidence which supports this in the case of calotropagenin. The difference in the molecular rotation of cardenolides with substituents CHO and CH_2·OH at position 10 is greater when rings A/B are *trans* than when they are *cis*. The difference in $[M_D]$ values



for calotropagenin and dihydrocalotropagenin is in reasonable agreement with that observed for *trans*-compounds (see Table)

Substance	A/B ring	10-Subst.	$[M]_D$ *	Δ
Gofruside } *a*	*trans*	CHO	−27°	65°
Frugoside } *a*	,,	CH_2·OH	−92	—
Corotoxigenin } *a, b*	,,	CHO	+163	73
Coroglaucigenin } *a, b*	,,	CH_2·OH	+90	—
Calotropagenin	—	CHO	+170	81
Dihydrocalotropagenin	—	CH_2·OH	+89	—
α-Antiarin } *c*	*cis*	CHO	−23	28
Dihydro-α-antiarin } *c*	,,	CH_2·OH	−51	—
Strophanthidin } *d*	,,	CHO	+175	16
Dihydrostrophanthidin } *d*	,,	CH_2·OH	+159	—

* Limits of error approx. ±8.[a]

[a] Hunger and Reichstein, *Helv. Chim. Acta*, 1952, **35**, 1073. [b] Stoll, Pereira, and Renz, *ibid.*, 1949, **32**, 293. [c] Doebel, Schlittler and Reichstein, *ibid.*, 1948, **31**, 688. [d] Rabald and Kraus, *Z. physiol. Chem.*, 1940, **265**, 39.

Experimental

M. p.s were determined by means of a Kofler block. Rotations refer to chloroform solutions at 28—30° except where other solvents are specified. Ultraviolet spectra were determined for ethanol solutions on a Beckman spectrophotometer, model D.U. Infrared spectra were measured with potassium bromide discs. We are grateful to Dr. S. M. Nagy, Massachusetts Institute of Technology, for the determinations of infrared absorption spectra and to Dr. F. Pascher, Bonn, for the microanalyses.

Isolation of the Cardiac Glycosides.—The experiments were on plant material obtained from *Calotropis procera* shrubs growing on the Pallisadoes peninsular, near Kingston, Jamaica. In preliminary experiments latex, leaves, and stalks, or root bark were examined separately. The last proved to be the most convenient source of glycosides, the following procedure being the best found. The bark (43·3 kg.) from freshly collected roots was cut into small pieces and made into a thin slurry with toluene-saturated water by means of a Waring blendor. After 24 hr., the slurry was filtered and the solid residue was left for a further 24 hr. just covered with toluene-saturated water. The residue obtained on filtration did not give a Raymond reaction. Both the first (36 l.) and the second (22 l.) filtrate were extracted in 3 l. portions, each with 6 × 3 l. of chloroform–ethanol (2 : 1). The chloroform extracts were combined, washed with 5% sodium hydrogen carbonate solution and water, dried, and evaporated. The residue was taken up in chloroform (200 c.c.) and treated with light petroleum (1 l.) to separate the steroid glycosides from plant resins which remained in solution. After repetition of this process the amorphous precipitates were combined (28 g.) and crystallised from ethanol, to give plates (3·9 g.), m. p. 238—248° (decomp.). This crystalline product (A) and the amorphous residue (B) obtained on evaporation of the filtrate contained combined nitrogen and sulphur (Lassaigne test; sodium plumbite test). Extracting product A (7·58 g.) successively with hot chloroform (2 × 100 c.c.) and methanol (2 × 50 c.c.) gave a relatively insoluble fraction (2·54 g.). This material on fractional elution chromatography on a column of silica gel (125 g.) with successively

chloroform–dioxan (10 : 1; 1 l.), chloroform (6 × 1 l.), and ethyl acetate (1 l.) gave uniform material in the last four chloroform fractions and in the ethyl acetate fraction. These fractions were combined and recrystallised from ethanol, to give plates, m. p. 265—271°, $[\alpha]_D$ +66° ± 3° [*c* 0·77 in chloroform–methanol (2 : 1)], $\lambda_{max.}$ 309, 217 mμ (log ε 1·49, 4·22) (Found: C, 63·2; H, 7·7. Calc. for $C_{29}H_{40}O_{10}$: C, 63·5; H, 7·4%). It has the same crystalline form as, and did not depress the m. p. of a sample of, calotoxin, m. p. 250—256°, kindly supplied by Professor G. Hesse. The acetate and benzoate were amorphous.

Attempts to separate the constituents of the amorphous product B, and the mother-liquors from the crystallisation of fraction A, by crystallisation and chromatography were impeded by the formation of mixed crystals and the rearrangements that took place when at least one of the constituents came in contact with columns of alumina and silica gel (see below). Lassaigne and sodium plumbite tests showed that both fractions contained nitrogen and sulphur. To simplify the separation the crude mixtures were separately treated with mercuric chloride in acetone, to remove nitrogen and sulphur.[10] The amorphous product obtained in this way from fraction B (37·2 g.) yielded crystals (6·1 g.) from ethanol. Similar treatment of the chloroform-soluble portion (7·8 g.) from fraction A gave crystals (5·2 g.). The crystalline material from both sources was mixed and fractionated by means of chloroform. The less soluble portion had properties similar to those of calotoxin. The chloroform-soluble fraction was identified as calactin, rectangular plates, m. p. and mixed m. p. (with calactin kindly supplied by Professor G. Hesse) 215—218°, $[\alpha]_D$ +45° ± 2° (*c* 1·2 in methanol), $\lambda_{max.}$ 301, 219 mμ (log ε 1·65, 4·19) [Found (for material dried over P_2O_5 at 130° *in vacuo*): C, 64·9; H, 7·4. Calc. for $C_{29}H_{40}O_9$: C, 65·3; H, 7·6%]. The *oxime*, prepared both from calactin kindly supplied by Professor G. Hesse and from our preparation, by the interaction (1 hr.) at 30° of the glycoside, hydroxylamine hydrochloride, and sodium acetate in methanol, had m. p. 280—284° (decomp.) [Found (for material dried over P_2O_5 at 130° *in vacuo*): C, 61·3; H, 7·5; N, 2·2. $C_{29}H_{41}O_9N,H_2O$ requires C, 61·6; H, 7·7; N, 2·5%]. Crystalline material could not be obtained when the more vigorous conditions described by Hesse *et al.*[3] were employed.

Calactinic Acid.—Calactin (52 mg.) in chloroform was applied to a column of alumina (2 g.) and left for 12 hr. Elution with methanol and chloroform–methanol–water (5 : 5 : 2) gave material (12 mg.) which was not characterised. Elution with chloroform–methanol–water (5 : 5 : 2) to which 1% of acetic acid had been added gave *calactinic acid* which crystallised from ethanol–chloroform as prisms (30 mg.), m. p. 170—173° (decomp.), $[\alpha]_D$ −24° ± 2° [*c* 0·92 in chloroform–methanol (2 : 1)], $\lambda_{max.}$ 309, 217 mμ (log ε 1·39, 4·2) [Found (for material dried at 80° over P_2O_5 *in vacuo*): C, 61·2; H, 7·6. $C_{29}H_{40}O_{10},H_2O$ requires C, 61·5; H, 7·5. $C_{29}H_{42}O_{10},H_2O$ requires C, 61·3; H, 7·8. Found (for material dried at 120° over P_2O_5 *in vacuo*): C, 62·8; H, 7·4. $C_{29}H_{40}O_{10}$ requires C, 63·5; H, 7·4. $C_{29}H_{42}O_{10}$ requires C, 63·3; H, 7·7%]. There was evidence of decomposition with release of carbon dioxide on continued drying. The *acetate* crystallised as needles, m. p. 174—176° (from ethanol–water), $[\alpha]_D$ −61° ± 2° (*c* 1·07) [Found: C, 61·2; H, 7·3; O, 32·0; OAc, 13·7. $C_{29}H_{38}O_{10}(C_2H_3O)_2,H_2O$ requires C, 60·9; H, 7·1; O, 32·0; OAc, 13·2%. $C_{29}H_{40}O_{10},(C_2H_3O)_2H_2O$ requires C, 60·7; H, 7·4; O, 31·9; OAc, 13·2%].

Reaction of Calactin with Activated Silica Gel.—In attempts to purify crude calactin by chromatography it was modified by contact with silica gel. *E.g.*, calactin (261 mg.) in benzene was added to a column of silica gel (20 g.) which had been freshly activated *in vacuo* at 220° for 40 min. The column was eluted successively with benzene, benzene–chloroform (1 : 1), chloroform, chloroform–ethyl acetate (1 : 1), ethyl acetate, and methanol during 4—8 hr. Traces of unchanged calactin and amorphous impurities were obtained from the benzene–chloroform and the methanol eluate, respectively. The major *component* (230 mg.), which was isolated principally from the chloroform–ethyl acetate eluate, crystallised as needles, m. p. 305—307° (from dioxan–water), $[\alpha]_D$ +54° ± 1° [*c* 1·62 in chloroform–methanol (2 : 1)], $\lambda_{max.}$ 310, 218 mμ (log ε 1·49, 4·23). [Found (for material dried over P_2O_5 at 130° *in vacuo*: C, 65·7; H, 7·6. $C_{29}H_{40}O_9$ requires C, 65·4; H, 7·6%]. The *benzoate* crystallised only after chromatography on alumina (quick elution), as plates, m. p. 195—200°, from acetone–ether [Found (material dried at 80° *in vacuo*): C, 67·3; H, 6·7. $C_{29}H_{39}O_9,C_7H_5O$ requires C, 67·9; H, 7·0%].

When the product of m. p. 305—307° (38 mg.), in methanol–chloroform (2 : 1; 2 c.c.), was left in contact with acid-washed, activated alumina for 20 hr. and then filtered, neutral material

[9] Ref. *a* of Table.
[10] Hesse and Gampp, *Chem. Ber.*, 1952, **85**, 933.

(15 mg.) was obtained from the filtrate. The alumina gave calactinic acid (18 mg.) when it was eluted with chloroform–methanol–water (5 : 5 : 2) containing acetic acid (1%). Repetition of the process with the neutral fraction gave a further yield of calactinic acid.

Preparation of Calotropagenin from Calactinic Acid.—Calactinic acid (4·17 g.) was refluxed for 11 hr. with 0·05N-sulphuric acid (250 c.c.) and methanol (250 c.c.). Pure nitrogen was passed through the mixture to sweep carbon dioxide formed into 0·1N-barium hydroxide. Titration indicated 0·6 mol. of carbon dioxide. Methanol was then removed by evaporation *in vacuo*. The aqueous solution was extracted with chloroform–ethanol (9 : 1), and the combined extracts were washed with water, 10% aqueous sodium carbonate solution, and water. A neutral product (3·0 g.) was obtained by evaporation of the chloroform extract. A small quantity (0·35 g.) of unchanged calactinic acid was obtained from the sodium carbonate washings. The aqueous solution and washings were mixed and treated with 2 : 4-dinitrophenylhydrazine (2·0 g.) in N-sulphuric acid (600 c.c.). After 24 hr. the precipitate was filtered off and dried (0·86 g.). Chromatography on alumina separated a variety of 2 : 4-dinitrophenylhydrazones. A major *component* had m. p. 257—259° (Found: C, 42·7; H, 3·3; N, 23·7. $C_{17}H_{16}O_9N_8$ requires C, 42·8; H, 3·4; N, 23·5%).

The neutral fraction from the hydrolysis was introduced in chloroform (300 c.c.) on to a column (2·5 × 25 cm.) of acid-washed alumina (Spence, Type H), which had been activated at 110° for 20 hr. The column was eluted with 500 c.c. portions of chloroform–ethyl acetate (1 : 1), ethyl acetate (8 portions), ethyl acetate–ethanol (5 : 1), ethyl acetate–ethanol (1 : 1), ethanol (2 portions), and chloroform–methanol–water (2 : 2 : 1). The ethyl acetate fractions contained mixtures. The eluates containing ethanol were evaporated, to yield *calotropagenin* (1·87 g.) which recrystallised from ethanol as conglomerates, m. p. 238—250°, $[\alpha]_D$ +43° ± 2° [*c* 1·21 in chloroform–methanol (2 : 1)], $\lambda_{max.}$ 218, 309 mμ (log ε 4·24, 1·38) (Found: C, 68·2; H, 8·1. Calc. for $C_{23}H_{32}O_6$: C, 68·3; H, 8·0%). Hesse and Reicheneder [2] gave m. p. 240° and $[\alpha]_D$ +42°. Calotropagenin did not react with periodic acid during 56 hr. The amorphous product obtained when calotropagenin was heated with concentrated hydrochloric acid did not have an absorption maximum at 315—250 mμ.

Reduction of Calotropagenin with Sodium Borohydride.—Calotropagenin (385 mg.) was reduced with sodium borohydride (120 mg.) in 40% aqueous tetrahydrofuran during 5 hr. The mixture was worked up in the usual way, to give a crude product (318 mg.) which on recrystallisation from ethanol gave pure *dihydrocalotropagenin* as plates (240 mg.), m. p. 268—273°, $[\alpha]_D$ +21° ± 3° (Found: C, 67·9; H, 8·4. $C_{23}H_{34}O_6$ requires C, 68·0; H, 8·4%). The Legal and the Raymond reaction were positive. The *triacetate*, prepared by acetic anhydride in pyridine, crystallised from acetone–ether as needles, m. p. 257—258°, $[\alpha]_D$ −19° ± 2° (*c* 1·18) (Found: C, 65·7; H, 7·6; OAc, 22·9. $C_{29}H_{40}O_9$ requires C, 65·4; H, 7·2; 3OAc, 26%). The *tribenzoate* crystallised from acetone as plates, m. p. 258—262°, $[\alpha]_D$ −15° ± 2° (*c* 1·21) (Found: C, 73·1; H, 6·5. $C_{44}H_{46}O_9$ requires C, 73·5; H, 6·5%).

Oxidation of Dihydrocalotropagenin with Chromium Trioxide.—The dihydrogenin (84 mg.) in acetic acid (5 c.c.) was treated with five portions of chromium trioxide (total 70 mg.) at intervals of 15 min. The mixture was kept for 12 hr., then worked up in the usual way to remove chromium compounds. The crude product was separated into acidic and neutral fractions with saturated aqueous sodium hydrogen carbonate. The acidic *product* crystallised from acetone as rhombohedra, m. p. 277—180° (Found: C, 65·0; H, 7·3. $C_{23}H_{28}O_7$ requires C, 66·3; H, 6·8%).

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University College of the West Indies, Jamaica. [*Received, August 18th*, 1958.]

XUM

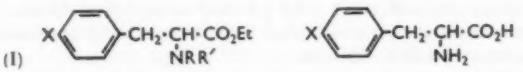
19. *Cyto-active Amino-acids and Peptides. Part V.*[1] *Derivatives of* p-*Amino- and* p-*Mercapto-phenylalanine.*

By F. Bergel and J. A. Stock.

A number of optically active *p*-alkyl- and *p*-aralkyl-aminophenylalanines has been prepared, three of which carry also the 2-chloroethyl group. *p*-2-Chloroethylamino-L-phenylalanine was obtained as its ethyl ester. *p*-2-Chloroethylthio-L-phenylalanine has been synthesised *via* *p*-mercapto-L-phenylalanine (L-thiotyrosine) and the *S*-2-hydroxyethyl derivative. The results of some biological tests are given.

The relatively high activity of difunctional " nitrogen mustard " derivatives of phenylalanine [2,3,4] and higher homologues [5] against the Walker rat carcinoma 256 and their effects on circulating leucocytes [6,7] prompted the synthesis of some monochloro- (" monofunctional ") and halogen-free (" non-functional ") analogues. It was hoped that such compounds might show more pronounced effects than other " monofunctional " agents not having an amino-acid structure.

The starting material for the compounds listed in the Table was *p*-nitro-*N*-phthaloyl-L- or -D- or *N*-acetyl-*p*-nitro-L-phenylalanine ethyl ester (I; X = NO_2, RR′ = phthaloyl; or R = H, R′ = Ac) described previously.[2,3] The secondary amines (I; X = NHEt, $NHPr^n$, and $Ph{\cdot}CH_2{\cdot}NH$, RR′ = phthaloyl) required for the synthesis of the three chloroethylamino-compounds (Nos. 1, 2, and 3) were prepared from the primary amine (I;



X = NH_2, RR′-phthaloyl) which has now been obtained crystalline in both its L- and its D-form, without preliminary purification as the hydrochloride.[2] When this amine was heated with ethanol and propan-1-ol in the presence of Raney nickel,[8,9] the amines (I; X = NHEt and $NHPr^n$, RR′ = phthaloyl) were formed. While a heating time of 2 hr., as given by Ainsworth,[9] was satisfactory for the higher alcohol, this was insufficient for the ethylamino-compound, which had to be heated with Raney nickel for at least 4 hr. to ensure complete absence of the initial primary amine. Boiling for only 2 hr. led to an apparently pure material which was converted into a biologically active chloroethyl compound. However, the observed anti-tumour effect was found to be due to contamination by the di-(2-chloroethyl) derivative [II; X = $(Cl{\cdot}CH_2{\cdot}CH_2)_2N$; CB 3025] formed from small amounts of primary amine (I; X = NH_2, RR′ = phthaloyl) whose presence was revealed by a positive diazotisation and coupling test of the intermediate (I; X = NHEt, RR′ = phthaloyl). This impurity could not be removed satisfactorily by recrystallisation. On the other hand prolonged heating had the disadvantage of lowering the yield and causing slight contamination with the tertiary amine (I; X = NEt_2, RR′ = phthaloyl) which was, however, eliminated during the subsequent stages.

The ethylamine (I; X = NHEt, RR′ = phthaloyl) was also prepared from the nitro-compound (I; X = NO_2, RR′ = phthaloyl) by catalytic reductive ethylation.[10] Alkylation by this method was, however, not always satisfactory. Moreover, a diazotisation

[1] Part IV, Bergel and Stock, *J.*, 1957, 4563.
[2] *Idem*, *J.*, 1954, 2409.
[3] Bergel, Burnop, and Stock, *J.*, 1955, 1223.
[4] Bergel and Stock, *Brit. Emp. Cancer Camp. Ann. Rep.*, 1953, **31**, 6.
[5] Davis, Roberts, and Ross, *J.*, 1955, 890.
[6] Elson, *Ann. New York Acad. Sci.*, 1958, **68**, 826.
[7] Elson, Talbot, Cardinali, and Lotz, *Brit. Emp. Cancer Camp. Ann. Rep.*, 1957, **35**, 58.
[8] Rice and Kohn, *J. Amer. Chem. Soc.*, 1955, **77**, 4052.
[9] Ainsworth, *ibid.*, 1956, **78**, 1635.
[10] Emerson, " Organic Reactions," Wiley, New York, 1948, Vol. IV, p. 174.

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and coupling test indicated that the crystalline product was again contaminated with traces of primary amine (I; X = NH_2, RR′ = phthaloyl). Attempts to prepare the derivative (I; X = NHEt, RR′ = phthaloyl) by catalytic reductive alkylation of the amine (I; X = NH_2, RR′ = phthaloyl) were unsuccessful. The intermediate benzylamine (I; X = Ph·CH_2·NH, RR′ = phthaloyl) was prepared by hydrogenation over Raney nickel of the Schiff's base (I; X = Ph·CH:N, RR′ = phthaloyl). The secondary bases were submitted to hydroxyethylation, chlorination, and hydrolysis in the usual

No.	Compound	CB no.	Isomer	Cryst. from	M. p.*	$[\alpha]_D$	Yield (%)
1	II; X = Cl·CH_2·CH_2·NEt	3135	L	—[a]	186—187°	−33°[b] +6·5[c]	37[d]
2	II; X = Cl·CH_2·CH_2·NPr^n	3155	L	—[a]	175—176	+3·5[f]	58[d]
3	II; X = Cl·CH_2·CH_2·N·CH_2Ph	3153	L	—[a]	173—175	+16[g]	34[d]
4	I; X = Cl·CH_2·CH_2·NH, R = R′ = H (dihydrochloride)	3198	L	E[j]	159—162	+26[k]	75
5	II; X = NMe_2	3167	L	A[h]	206 208	−40[i]	61
6	II; X = NMe_2	3192	D	A[h]	206—207	+41[i]	51
7	II; X = NHEt	3165	L	B[j]	215—217	−38[k]	53
8	II; X = NEt_2	3193	L	B[j]	183—184	+9[l]	33
9	II; X = Ph·CH_2·NH	3194	L	C[m]	214—216	+14[p]	75
10	II; X = HS (hydrochloride)	3195	L	D[j]	231—233	−4[q]	37[r]
11	II; X = HO·CH_2·CH_2·S (hydrochloride)	3196	L	—[s]	193—196	−6[t]	85
12	II; X = Cl·CH_2·CH_2·S (hydrochloride)	3175	L	D[j]	197—200	+16[u]	94

No.	Formula	Found (%) C	H	N	S	Cl	Required (%) C	H	N	S	Cl
1	$C_{13}H_{19}O_2N_2Cl$[a]	57·7	7·3	10·0	—	13·0	57·6	7·1	10·35	—	13·1
2	$C_{14}H_{21}O_2N_2Cl$[a]	59·0	7·3	9·7	—	12·2	59·0	7·4	9·8	—	12·5
3	$C_{18}H_{21}O_2N_2Cl,H_2O$	62·0	6·7	8·0	—	10·3	61·6	6·6	8·0	—	10·1
	$C_{18}H_{21}O_2N_2Cl$[a]	—	—	8·2	—	10·7	—	—	8·4	—	10·7
4	$C_{13}H_{19}O_2N_2Cl,2HCl$[w]	46·0	6·3	8·1	—	—	45·4	6·2	8·15	—	—
5	$C_{11}H_{16}O_2N_2$	63·5	7·95	13·4	—	—	63·4	7·7	13·45	—	—
6	,,	,,	7·9	13·2	—	—	,,	,,	,,	—	—
7	,,[x]	63·25	,,	13·45	—	—	,,	,,	,,	—	—
8	$C_{13}H_{20}O_2N_2,\frac{1}{2}H_2O$[yz]	64·5	8·6	11·6	—	—	64·4	8·6	11·6	—	—
		64·2	8·4	11·6	—	—					
9	$C_{16}H_{18}O_2N_2$[a]	71·3	6·8	10·6	—	—	71·1	6·7	10·4	—	—
10	$C_9H_{11}O_2NS,HCl$	45·9	5·5	5·9	13·7	—	46·2	5·2	6·0	13·7	—
11	$C_{11}H_{15}O_2NS,HCl$	46·8	5·7	4·9	12·0	—	47·5	5·8	5·0	11·5	—
12	$C_{11}H_{14}O_2NSCl,HCl$	44·4	5·2	4·65	—	—	44·6	5·1	4·7	—	—

* All the compounds melted with decomposition.

A, Aq. MeOH. B, MeOH–EtOH. C, Aq. EtOH. D, Conc. HCl. E, EtOH–Et_2O.

[a] Purified by repptn. (Expt. section). [b] *c* 1·25 in MeOH at 23°. [c] *c* 2·2 in N-HCl at 21°. [d] Calc. on the intermediate *p*-monoalkylamino-N^α-phthaloylphenylalanine ester. [e] Compound dried 3—4 hr. at 110°/0·5 mm. [f] *c* 1·95 in N-HCl at 25°. [g] *c* 2·36 in N-HCl at 25°. [h] Slightly tinted plates. [i] *c* 1·0 in 0·1M-phosphate buffer (pH 7) at 22°. [j] Colourless or slightly tinted prisms [k] *c* 3·29 in H_2O at 24°. [l] *c* 2·20 in N-HCl at 25°. [m] Analytical figures given for two separate preparations. [n] Colourless needles. [p] *c* 2·77 in N-HCl at 24°. [q] *c* 2·35 in N-HCl at 25°. [r] Calc. on the intermediate *N*-acetyl-*p*-nitrophenylalanine ester. [s] Precipitated from solution in MeOH or EtOH by addition of Et_2O. [t] *c* 3·0 in H_2O at 24°. [u] *c* 3·7 in EtOH at 22°. [v] *c* 0·35 in MeOH at 25°. [w] Dried 30 min. at 90°/1 mm.

manner [2] and gave the three *N*-chloroethyl-*N*-alkyl- or -benzyl-amino-L-phenylalanines (Nos. 1, 2, 3).

When the crude non-crystalline intermediate (I; X = HO·CH_2·CH_2·NH·CH_2Ph, RR′ = phthaloyl) was hydrogenolysed over palladium–charcoal, the 2-hydroxyethylamino-compound (I; X = HO·CH_2·CH_2·NH, RR′ = phthaloyl) was formed. A similar reaction with the free amino-acid (II; X = Cl·CH_2·CH_2·NH·CH_2Ph) led to a crystalline deliquescent hydrochloride which was characterised as the analytically pure hydrochloride of the ester (I; X = Cl·CH_2·CH_2·NH, R = R′ = H).

Several "non-functional" analogues were synthesised for comparative biological purposes (Nos. 5, 6, 7, 8, and 9). The preparation of *p*-dimethylamino-DL-phenylalanine

by an azlactone synthesis has been reported by others.[11] *p*-Dimethyl- and *p*-diethylamino-phenylalanine have been claimed by Harper *et al.*[12] but these authors do not indicate the method of preparation or the configuration of the compounds, nor do they give analytical or physical data. We prepared the *p*-dimethylamino-L- and -D-phenylalanine (II; X = NMe_2) by catalytic reductive methylation of the nitro-compound (I; X = NO_2, RR′ = phthaloyl) and subsequent hydrolysis. An attempted dimethylation of the amine (I; X = NH_2, RR′ = phthaloyl) by the Eschweiler–Clarke modification of the Leuckart reaction,[13] using formaldehyde and formic acid, gave an intractable gum. *p*-Ethylamino-L-phenylalanine (II; X = NHEt) was prepared by hydrolysis of the intermediate (I; X = NHEt, RR′ = phthaloyl) discussed above, and was purified by chromatography on powdered cellulose. Catalytic reductive diethylation [10] of the nitro-compound (I; X = NO_2, RR′ = phthaloyl) with acetaldehyde gave a non-crystalline product which yielded, on hydrolysis, a crude granular hydrochloride. Paper chromatography revealed the presence of a substantial quantity of a fast-moving impurity, together with the required diethylamine II; X = NEt_2) and a trace of the primary amine (II; X = NH_2). The major impurity was possibly a higher alkyl derivative of *p*-aminophenylalanine formed from a polymer of acetaldehyde, but no attempt has been made to isolate this substance. Pure *p*-diethylamino-L-phenylalanine was obtained by chromatography on cellulose and subsequent crystallisation. *p*-Benzylamino-L-phenylalanine (II; X = $Ph{\cdot}CH_2{\cdot}NH$) was readily prepared by hydrolysis of the corresponding phthaloyl ester.

The synthesis of the " hemi-sulphur mustard " L-derivative (II; X = $Cl{\cdot}CH_2{\cdot}CH_2{\cdot}S$) involved the initial preparation of *p*-mercapto-L-phenylalanine. For this, we employed the diazonium xanthate method used recently by Colescott, Herr, and Dailey [14] in the preparation of the DL-form from a malonic ester intermediate. Our first experiments started with the L-phthaloyl derivative (I; X = NH_2, RR′ = phthaloyl) but hydrolysis of the product was unsatisfactory. We therefore employed the L-acetyl compound [3] (I; X = NH_2, R = H, R′ = Ac) which was diazotised and then converted into the xanthate (I; X = $EtO{\cdot}CS_2$, R = H, R′ = Ac) and thence into the hydrochloride of the *p*-mercapto-L-phenylalanine (II; X = SH), best purified through the mercuric chloride complex. Reaction of this thiol with ethylene oxide at room temperature in the presence of excess of sodium hydrogen carbonate proceeded rapidly without involving the α-amino-group significantly, conversion into the hydroxyethyl derivative (II; X = $HO{\cdot}CH_2{\cdot}CH_2{\cdot}S$) being practically complete in about 2 min. Brief heating of this compound with concentrated hydrochloric acid [15] gave the hydrochloride of the " hemi-sulphur mustard " (II; X = $Cl{\cdot}CH_2{\cdot}CH_2{\cdot}S$).

In tests on the Walker rat carcinoma 256, the " monofunctional " derivatives, CB 3135, 3153, 3155, and 3175 (see Table) appeared much less effective than the corresponding difunctional compound, *p*-di-(2-chloroethyl)amino-L-phenylalanine [II; X = $(Cl{\cdot}CH_2{\cdot}CH_2)_2N$] (CB 3025, Melphalan),[4] without showing on the whole a corresponding decrease in toxicity in the animal not bearing a tumour. The first sample of CB 3135, which has one chlorine atom less than Melphalan, produced anti-timour effects at ten times the dose of the latter (1 mg./kg.) but, as outlined above, this was due to contamination by the di-(2-chloroethyl) analogue. Pure CB 3135 was inactive below the toxic dose (75 mg./kg.), even though its chemical reactivity as measured by its rate of hydrolysis at pH 7 and 37° (determination by Dr. W. Davis) was about four times that of CB 3025. A mixture of the latter and CB 3135 (0·25 mg./kg.; 25 mg./kg.) proved equally ineffective. This suggested that contamination of the first sample of CB 3135 by CB 3025 exceeded 1%, indicating an enrichment of the " difunctional " impurity during the final stages of the synthesis. While the benzyl compound CB 3153 exerted some activity at 150 mg./kg.,

[11] Elliott, Fuller, and Harington, *J.*, 1948, 85.
[12] Harper, Furst, and Morris, *Wasmann J. Biol.*, 1950, **8**, 299.
[13] Moore, " Organic Reactions," Wiley, New York, 1949, Vol. V, p. 301.
[14] Colescott, Herr, and Dailey, *J. Amer. Chem. Soc.*, 1957, **79**, 4232.
[15] Connors and Ross, *Chem. and Ind.*, 1958, 366.

the propyl derivative CB 3155 at 150 mg./kg. and the " half-sulphur mustard " CB 3175 at 10 mg./kg. (toxic at 25 mg./kg.) were inactive. The last result is the more interesting as the " half-sulphur mustard " $HO{\cdot}CH_2{\cdot}CH_2{\cdot}S{\cdot}CH_2{\cdot}CH_2Cl$ showed some promise in clinical trials.[16] However, in general, difunctionality seems necessary for substantial activity, as with other " mustard derivatives." [17] Of the " non-functional " phenylalanine derivatives, CB 3167 was tested with negative results.

Experimental

p-*Amino*-N$^{\alpha}$-*phthaloyl*-L- *and* D-*phenylalanine Ethyl Ester* (I; X = NH_2, RR′ = phthaloyl). —These compounds were originally characterised as the hydrochlorides.[2] Each has now been obtained crystalline as the free base directly from the (palladium–charcoal) hydrogenation product of the corresponding nitro-compound. The L-*amine* crystallised from aqueous methanol, in yellow prisms (91%), m. p. 102—103°, $[\alpha]_D^{21}$ −213° (*c* 1·0 in EtOH) (Found: C, 67·4; H, 5·3; N, 8·2. $C_{19}H_{18}O_4N_2$ requires C, 67·4; H, 5·4; N, 8·3%). The D-*amine* (90%) had m. p. 102—104°, $[\alpha]_D^{23}$ +212° (*c* 1·0 in EtOH) (Found: N, 8·2%).

p-*Ethylamino*-N$^{\alpha}$-*phthaloyl*-L-*phenylalanine Ethyl Ester* (I; X = NHEt, RR′ = phthaloyl).—(*a*) *p*-Nitro-*N*-phthaloyl-L-phenylalanine ethyl ester [2] (7·4 g., 0·02 mol.) and acetaldehyde (1·4 ml., 0·025 mol.) were hydrogenated in ethanol (200 ml.) in the presence of anhydrous sodium acetate (0·4 g., 0·005 mol.) over Raney nickel (2 g.) and Adams platinum catalyst (0·2 g.) (cf. Emerson [10]). Hydrogen uptake was complete in a few hours. Evaporation of the filtrate to a smaller volume gave the *ester* as yellow prisms (5·95 g., 81%), m. p. 124—126° (unchanged on recrystallisation from ethanol), $[\alpha]_D^{22}$ −226° (*c* 0·47 in dioxan) (Found: C, 68·9; H, 6·05; N, 7·65. $C_{21}H_{22}O_4N_2$ requires C, 68·8; H, 6·05; N, 7·65%). A diazotisation and coupling test, carried out as in (*b*), indicated very slight contamination by the primary amine (I; X = NH_2, RR′ = phthaloyl).

(*b*) In one experiment, *p*-amino-N$^{\alpha}$-phthaloyl-L-phenylalanine ethyl ester (5·0 g.), ethanol-moist Raney nickel (17 g.), and ethanol (45 ml.) were heated for 2 hr. under reflux with stirring (cf. Rice and Kohn [8] and Ainsworth [9]). The hot mixture was filtered through " Hyflo " and evaporated to a smaller volume. The cooled solution deposited yellow prisms (4·8 g., 89%) of the ester, m. p. 126—128°, mixed m. p. of 124—126° with the product described in (*a*) (Found: C, 68·9; H, 6·25; N, 7·65%). The material (m. p. 126—128°) gave a pink colour when treated with nitrite in acid solution, then with an alkaline solution of R-acid (2-naphthol-3 : 6-disulphonic acid). A control experiment, in which the amine was omitted, gave no colour. The intensity of the colour indicated contamination by not more than *ca.* 0·5% of primary amine. Recrystallisation from ethanol did not remove the colour-producing material.

Heating the primary amine with the Raney-nickel for a longer period (4—6 hr.) gave a somewhat lower yield (*ca.* 70%), and the recrystallised product had a lower m. p. (123—126°). It was, however, free from primary amine (diazotisation and R-acid coupling test), though the experiments in which it was hydrolysed to the free amino-acid (II; X = NHEt) (see below) indicated slight contamination by the tertiary amine (I; X = Et_2N, RR′ = phthaloyl).

p-n-*Propylamino*-N$^{\alpha}$-*phthaloyl*-L-*phenylalanine Ethyl Ester* (I; X = $NHPr^n$, RR′ = phthaloyl).—The method of preparation was as above, except that propan-1-ol was used instead of ethanol. The heating time was 4·5 hr. The gummy product crystallised from methanol in yellow prisms (0·44 g., 78%) of the *ester*, m. p. 94—97°. Recrystallisation from methanol raised the m. p. to 97—98° and the pure compound had $[\alpha]_D^{22}$ −202° (*c* 1·62 in EtOH) (Found: C, 69·1; H, 6·6; N, 7·3. $C_{22}H_{24}O_4N_2$ requires C, 69·45; H, 6·4; N, 7·4%).

p-*Benzylideneamino*-N$^{\alpha}$-*phthaloyl*-L- *and* -D-*phenylalanine Ethyl Ester* (I; X = Ph·CH:N, RR′ = phthaloyl).—*p*-Amino-N$^{\alpha}$-phthaloyl-L-phenylalanine ethyl ester (6·0 g.), benzaldehyde (2·4 ml., 1·3 mol. equiv.), anhydrous sodium acetate (0·5 g.), and methanol (35 ml.) were heated 1 hr. under reflux. The *azomethine* crystallised, on cooling, as pale yellow prisms, m. p. 110—111°, unchanged on recrystallisation from methanol (6·55 g., 86%; the yield tended to be a little lower in the absence of sodium acetate), $[\alpha]_D^{24}$ −239° (*c* 0·90 in EtOH) (Found: C, 73·2; H, 5·3; N, 6·4. $C_{26}H_{22}O_4N_2$ requires C, 73·2; H, 5·2; N, 6·6%).

The D-*isomer* was prepared similarly in 75% yield from the corresponding primary amine.[2]

[16] Seligman and Rutenburg, *Ann. New York Acad. Sci.*, 1958, **68**, 1181.
[17] Haddow, Kon, and Ross *Nature*, 1948, **162**, 824.

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The product had m. p. 110—111°, $[\alpha]_D^{21}$ +246° (*c* 1·2 in EtOH) (Found: C, 73·05; H, 5·3; N, 6·6%).

p-*Benzylamino*-N$^{\alpha}$-*phthaloyl*-L- *and* -D-*phenylalanine Ester* (I; X = Ph·CH_2·NH, RR′ = phthaloyl).—The L-azomethine (6·53 g.) was hydrogenated at room temperature and pressure over Raney nickel in ethanol–ethyl acetate (1 : 1 by vol.; 100 ml.). The filtrate was evaporated, and the residual gum crystallised from methanol. The *benzylamine* formed colourless needles, m. p. 118—120° (5·87 g.; 90%), $[\alpha]_D^{21}$ −185° (*c* 1·58 in EtOH) (Found: C, 72·4; H, 5·5; N, 6·6. $C_{24}H_{24}O_4N_2$ requires C, 72·9; H, 5·65; N, 6·5%). The D-*benzylamine* was obtained similarly and had m. p. 118—120°, $[\alpha]_D^{21}$ +188° (*c* 0·98 in EtOH) (Found: N, 6·5%).

p-*Benzylamino*-L-*phenylalanine* (II; X = Ph·CH_2·NH).—*p*-Benzylamino-*N*$^{\alpha}$-phthaloyl-L-phenylalanine ethyl ester (1·6 g.) was heated for 4 hr. under reflux with 6N-hydrochloric acid (15 ml.). The solution became homogeneous within 45 min. The cooled solution was filtered from the phthalic acid and evaporated to dryness under vacuum, and the residue dissolved in water (5 ml.). Neutralisation with concentrated sodium acetate solution precipitated the crude *amino-acid* which was collected, washed with water, dried, and crystallised from aqueous ethanol (Table, No. 9).

p-(N-2-*Chloroethyl*-N-*ethyl*)-, p-(N-2-*Chloroethyl*-N-n-*propyl*)- *and* p-(N-*Benzyl*-N-2-*chloroethyl*)-*amino*-L-*phenylalanine* (II).—The hydroxyethylation and subsequent chlorination of *p*-ethyl-, *p*-*n*-propyl-, and *p*-benzyl-amino-*N*$^{\alpha}$-phthaloyl-L-phenylalanine ethyl ester were carried out with ethylene oxide and freshly distilled phosphorus oxychloride by the method used earlier for the "nitrogen-mustard" derivative of phenylalanine.[2] All the intermediate hydroxyethyl derivatives were gums. The chlorinated products were severally heated under reflux for 4 hr. with 6N-hydrochloric acid. The isolation, using sodium acetate, followed the published method.[2] Each of the products resisted crystallisation but was purified for analysis and biological testing by dissolution in excess of N-hydrochloric acid, precipitation from the filtered solution by the addition of N-sodium hydroxide and thorough washing of the precipitate with water (Nos. 1, 2, and 3).

The rates of hydrolysis of CB 3135 (II; X = Cl·CH_2·CH_2·NEt) and CB 3025 [II; X = (Cl·CH_2·CH_2)$_2$N] [2] at pH 7 and 37°, determined by Dr. W. Davis using a Pye automatic titrator, were: CB 3135, $k = 6{\cdot}66 \times 10^{-4}$ sec.$^{-1}$ (half-life 17·4 min.); CB 3025, $k = 1{\cdot}45 \times 10^{-4}$ sec.$^{-1}$ (half-life 79·7 min.).

p-2-*Chloroethylamino*-L-*phenylalanine Ethyl Ester* (I; X = Cl·CH_2·CH_2, R = R′ = H).—*p*-(*N*-Benzyl-*N*-2-chloroethyl)amino-L-phenylalanine (1·35 g.) was debenzylated by hydrogenation, at room temperature and pressure, in ethanol (10 ml.) containing 10N-ethanolic hydrogen chloride (0·4 ml., 1 equiv.). The granular product (0·85 g.), m. p. 129—131° (decomp.), obtained by addition of ether to the filtered mixture, was converted into colourless plates, m. p. 136—137°, by reprecipitation from ethanol. The compound became sticky on storage in a stoppered tube and gave an unsatisfactory analysis. The tetraphenylboron derivative was also hygroscopic. The compound was therefore converted into the *ester hydrochloride* with cold 10N-ethanolic hydrogen chloride (2 days at room temperature) (Table, No. 4).

p-2-*Hydroxyethylamino*-N$^{\alpha}$-*phthaloyl*-L-*phenylalanine Ethyl Ester* (I; X = HO·CH_2·CH_2·NH, RR′ = phthaloyl).—*p*-Benzyl-(2-hydroxyethyl)amino-*N*$^{\alpha}$-phthaloyl-L-phenylalanine ethyl ester was prepared, as mentioned above, by the usual procedure,[2] from the corresponding benzylamine (I; X = Ph·CH_2·NH, RR′ = phthaloyl) (2·2 g.). It did not crystallise but was successfully hydrogenolysed at ordinary temperature and pressure over 5% palladium–charcoal (3 g.) in ethanol (150 ml.). The *hydroxyethylamine* crystallised from aqueous methanol in pale yellow plates (1·32 g., 68%, calc. on the intermediate *p*-benzylamino-*N*$^{\alpha}$-phthaloyl-L-phenylalanine ethyl ester), m. p. 108—111°, $[\alpha]_D^{24}$ −194° (*c* 2·07 in EtOH). Recrystallisation from aqueous methanol raised the m. p. to 110—112° (Found: C, 65·85; H, 6·1; N, 7·2. $C_{21}H_{22}O_5N_2$ requires C, 65·95; H, 5·8; N, 7·3%).

p-*Dimethylamino*-N-*phthaloyl*-L- *and* -D-*phenylalanine Ethyl Ester* (I; X = Me_2N, RR′ = phthaloyl).—The conditions of Bowman and Stroud [16] were used. *p*-Nitro-*N*-phthaloyl-L-phenylalanine ethyl ester [2] (32 g.) and 40% aqueous formaldehyde (50 ml., 8 mol. equiv.) were hydrogenated in ethanol (480 ml.) over 5% palladium–charcoal (16 g.) in the presence of anhydrous sodium acetate (16 g., 2 equiv.). Approximately the theoretical volume (5 mol.) of hydrogen was absorbed. The filtrate and ethanol washings were evaporated until sodium acetate began to crystallise. Hot water was added to a faint turbidity, the sodium acetate

[16] Bowman and Stroud, *J.*, 1950, 1342.

redissolving. The cooled solution deposited yellow plates of the *dimethylamino-compound* (27 g., 85%), m. p. 120—122°, $[\alpha]_D^{21}$ −214° (*c* 1·0 in MeOH). Recrystallisation from a small volume of ethanol raised the m. p. to 123—124° (Found: C, 68·8; H, 6·15; N, 7·7. $C_{21}H_{22}O_4N_2$ requires C, 68·8; H, 6·05; N, 7·65%). The D-*isomer* was prepared in 84% yield in the same way from *p*-nitro-*N*-phthaloyl-D-phenylalanine ethyl ester.[3] It formed yellow plates, m. p. 123—124°, $[\alpha]_D^{21}$ +221° (*c* 1·0 in MeOH) (Found: C, 69·0; H, 6·05; N, 7·65%).

p-*Dimethylamino-*L- *and* -D-*phenylalanine* (II; X = NMe_2).—*p*-Dimethylamino-*N*-phthaloyl-L-phenylalanine ethyl ester (27·0 g.) was heated under reflux for 5 hr. with 6N-hydrochloric acid (200 ml.). Evaporation of the solution to smaller bulk, cooling, removal of phthalic acid, neutralisation with 4N-lithium hydroxide, and dilution with ethanol gave a crude product (13·2 g.) from which the pure L-*amino-acid* (9·3 g.) was obtained by crystallisation. The D-*amino-acid* was prepared similarly (Nos. 5 and 6).

p-*Ethylamino-*L-*phenylalanine* (II; X = NHEt).—In a preliminary experiment, a crystalline substance was obtained by the lithium hydroxide treatment of an ethanol solution of the hydrolysis product of *p*-ethylamino-N^{α}-phthaloyl-L-phenylalanine ethyl ester. The substance gave two ninhydrin-positive components when run on Whatman No. 1 paper with butan-1-ol–propan-1-ol–0·1N-aqueous ammonia (2 : 1 : 1 by vol.), the main spot having R_F 0·33, and the minor R_F 0·62 (= R_F of *p*-diethylaminophenylalanine). The second component was not removed by crystallisation from aqueous ethanol. The compound was therefore prepared and purified as follows.

p-Ethylamino-N^{α}-phthaloyl-L-phenylalanine ethyl ester (1·0 g.) was heated for 4 hr. under reflux with 6N-hydrochloric acid (15 ml.). The solution was cooled, filtered from the phthalic acid, and evaporated to dryness under a vacuum. The residue was dissolved in sufficient (1·5 ml.) 2N-aqueous ammonia to give a neutral solution, and diluted with butan-1-ol–propan-1-ol (2 : 1; 4·5 ml.). The mixture was placed on a powdered cellulose (80 g. dry wt.) column (37 × 3·5 cm.) made up in butan-1-ol–propan-1-ol–0·1N-aqueous ammonia (2 : 1 : 1). The column was eluted with the same solvent at *ca.* 2 ml. per min. The first 130 ml. of eluate were discarded and 7 ml. fractions were then collected. Fractions 31—52 inclusive contained ninhydrin-positive material of R_F 0·32 only (run on Whatman No. 1 in the same solvent), and were combined and evaporated. The crystalline white residual *amino-acid* was recrystallised (No. 7).

p-*Diethylamino-*L-*phenylalanine* (II; X = NEt_2).—*p*-Nitro-*N*-phthaloyl-L-phenylalanine ethyl ester [3] (10·0 g.) and acetaldehyde (10·5 ml., 7 mol. equiv.) were hydrogenated at room temperature and pressure in the presence of sodium acetate (0·5 g. anhydrous; 2 equiv.) over 5% palladium–charcoal (5 g.) in ethanol (250 ml.) containing water (15 ml.) (which appeared to assist the alkylation). Approximately the calculated volume (5 mol.) of hydrogen was absorbed. Evaporation of the filtrate and separation from sodium acetate by extraction into ether gave a gum.

Most (8 g.) of the gum was hydrolysed in the same way as the ethylamine analogue. The crude amino-acid hydrochloride (5·5 g.) was isolated in granular form by addition of ether to a solution in methanol, and subsequent trituration of the semisolid precipitate with ethyl acetate. Chromatography on Whatman No. 1 paper with butanol–propanol–0·1N-aqueous ammonia (2 : 1 : 1 by vol.) revealed three ninhydrin-positive components having R_F values 0·93, 0·63 (main component) and 0·35 (very faint; = R_F of *p*-aminophenylalanine) respectively. Part (1·45 g.) of the crude hydrochloride was run on a column similar to that used in the purification of *p*-ethylaminophenylalanine but containing a larger amount (175 g.) of cellulose. The first 300 ml. eluate were rejected, and 10 ml. fractions were then collected. Substantial overlap of the three components occurred but evaporation of combined fractions 24—36 (which contained the bulk of the required material of R_F 0·62) and crystallisation of the residue gave chromatographically pure p-*diethylamino-*L-*phenylalanine* (No. 8). Analysis of two preparations indicated that one-third of a mol. of water was strongly held. An attempted purification by ion-exchange chromatography on Amberlite IR 120 was unsatisfactory.

N-*Acetyl*-S-(*ethoxythiocarbonyl*)-p-*mercapto-*L-*phenylalanine Ethyl Ester* (I; X = Et·O·CS_2, R = H, R′ = Ac).—The method resembled that of Colescott *et al.*[14] *p*-Amino-N^{α}-acetyl-L-phenylalanine ethyl ester [3] (4·1 g. of gum) was dissolved in 6N-hydrochloric acid (15 ml.) and diazotised at 0—5° by the dropwise addition of a solution of sodium nitrite (1·5 g., 1·3 equiv.) in water (3 ml.). The slight excess of nitrous acid was destroyed by the addition of a crystal of sulphamic acid. The solution was carefully neutralised (pH 7) by the addition, with ice-cooling

XUM

and stirring, of powdered, anhydrous sodium carbonate. Potassium ethylxanthate (3·42 g., 1·3 mol.), dissolved in water (5 ml.), was added dropwise during about 5 min. to the cooled, stirred solution. The diazonium ethylxanthate was precipitated as a thick yellow gum. The mixture was heated for 50 min. with stirring at 60—70°, gas evolution occurring. The mixture was cooled, the gummy product extracted into ethyl acetate, the solution dried ($MgSO_4$), and the solvent removed under a vacuum. The residue (A; 5·2 g.) did not crystallise. However, in another similar experiment (not recorded in detail here because of complications due to substantial hydrolysis of the ethyl ester group, caused, it is believed, by having the solution too alkaline during the heating of the diazonium ethylxanthate solution) a crystalline neutral product (3·4 g., 30% calc. on the intermediate *p*-nitro-compound) was isolated by ether extraction. Recrystallisation from aqueous Cellosolve gave almost colourless needles of N-*acetyl*-S-(*ethoxythiocarbonyl*)-p-*mercapto*-L-*phenylanine ethyl ester*, m. p. 69—72°, $[\alpha]_D^{24}$ +25° *c* 0·99 in EtOH) (Found: C, 54·2; H, 6·1; N, 3·9. $C_{16}H_{21}O_4NS_2$ requires C, 54·1; H, 6·0; N, 3·9%).

p-*Mercapto*-L-*phenylalanine* (II; X = SH).—Most (4·6 g.) of the gummy ester (A above) was heated for 4 hr. under reflux with 6N-hydrochloric acid (30 ml.). The solution was evaporated to a smaller volume, then cooled. The colourless product (B) was collected, washed with a little concentrated hydrochloric acid, and dried (NaOH). It weighed 2·52 g., and an iodine titration indicated that it contained 45% of the required compound. The material was taken up in boiling 6N-hydrochloric acid (15 ml.), and zinc dust (1 g.) was added to the boiling solution in small quantities during 15 min. The solution was filtered, and concentrated hydrochloric acid (15 ml.) was added. The cooled solution yielded a crystalline substance (C; 1·95 g.) of improved iodine titre (67% of calc. SH); further treatment with zinc and acid did not improve this titre. The mother-liquors from (B) above gave, on further evaporation, a second crop of almost colourless crystals (D; 0·5 g.) having an iodine titre of 82% of theory. Materials (C) and (D) were sufficiently pure for conversion into the *S*-chloroethyl derivative described below. Analytically pure material was obtained by treatment of the mercuric chloride complex with hydrogen sulphide and final isolation as p-*mercapto*-L-*phenylalanine hydrochloride* (iodine titre *ca.* 99%) (No. 10).

p-2-*Hydroxyethylthio*-L-*phenylalanine* (II; X = $HO{\cdot}CH_2{\cdot}CH_2{\cdot}S$).—*p*-Mercapto-L-phenylalanine hydrochloride (0·50 g.), purified through the mercuric chloride complex, was added to air-free water (10 ml.) through which carbon dioxide was passing. Sodium hydrogen carbonate (1·0 g.) was added with shaking, then ethylene oxide (1 ml.). The solution was set aside for 10 min. (In a preliminary experiment it was found that the iodine titre of aliquot parts fell to zero quite rapidly, the reaction with ethylene oxide being practically complete in 1—2 min.) Concentrated hydrochloric acid (2·5 ml.) was added to the filtered solution which was evaporated to dryness under vacuum. The residue was heated with a little water on a steam-bath for 2 min. (to decompose any chloroethyl derivative which may have been present), the solution evaporated, the residue extracted with boiling ethanol, and the ethanol solution evaporated. The residue was taken up in methanol and precipitated by addition of ether, to give the *amino-acid hydrochloride* (0·50 g.) (No. 11). When the product was run on Whatman No. 1 paper, with butanol–propanol–propionic acid–water (10 : 5 : 2 : 5), only one ninhydrin-positive component was revealed (R_P 0·5).

p-2-*Chloroethylthio*-L-*phenylalanine* (II; X = $Cl{\cdot}CH_2{\cdot}CH_2{\cdot}S$).—*p*-2-Hydroxyethylthio-L-phenylalanine hydrochloride (0·5 g.) was suspended in concentrated hydrochloric acid (10 ml.) and heated to the b. p. Complete dissolution occurred. After 1 minute's further boiling, crystals began to separate, and the mixture set to a solid mass of colourless crystals within a further 0·5 min. The mixture was cooled at once (a longer heating period, with addition of acid to redissolve the product results in a lower yield), and the product was collected and washed with a little concentrated hydrochloric acid.

The *amino-acid hydrochloride* (0·5 g.) (No. 12) was analytically pure, and had R_P 0·7 in the system used with the parent hydroxy-compound. Paper chromatography also showed that complete reconversion into the hydroxy-compound occurred when an aqueous solution of the chloro-compound was boiled for 3 min. In ethanol, no hydrolysis was detected when the solution was heated at the b. p. for 1 min.

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Microanalytical Laboratories, the Imperial College of Science and Technology, and by Mr. P. R. W. Baker, the Wellcome Research Laboratories, Beckenham, Kent.

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20. *Cyto-active Amino-acids and Peptides. Part VI.*[1] *Synthesis of* N′-α-*Aminoacyl*-NN-*di*-(2-*chloroethyl*)-p-*phenylenediamines.*

By F. BERGEL and J. A. STOCK.

A number of *N*′-[α-(benzyloxycarbonylamino)acyl]-*NN*-di-(2-chloroethyl)-*p*-phenylenediamines and two derived α-aminoacyl compounds are described. Tests of the latter on experimental tumours failed to give promising results.

ROSS, WARWICK, and ROBERTS,[2] and HEBBORN and DANIELLI,[3,4] have reported on the chemistry and interesting biological properties of a series of *N*′-acyl-*NN*-di-(2-chloroethyl)-*p*-phenylenediamines. The design of these compounds was based on a working hypothesis of Danielli [5] and of Ross *et al.*[2] for selectivity of biological action. The experimental findings supported the idea that the blocking of the primary amino-group by acylation, and consequent deactivation of the " nitrogen mustard " group, could produce drugs with latent activity. Deacylation by enzymes within the neoplastic cell would then release the active parent compound at the right site. We have extended this work by undertaking the synthesis of some α-aminoacyl analogues of type (II).

The chloroformate mixed anhydride procedure [6,7] was used in the condensation of the benzyloxycarbonyl derivatives of glycine, DL-alanine, L-leucine, DL-methionine, and DL-phenylalanine with *NN*-di-(2-chloroethyl)-*p*-phenylenediamine. The benzyloxycarbonylamino-anilides (I; Nos. 1—5 of the Table) were thus obtained.

No.	Compound	Isomer	Cryst.¶ from	M. p.	Yield (%)
1	I; R = H	—	EtOH	144—145°	61
2	I; R = Me	DL	Aq. EtOH	126—127	44
3	I; R = $Me_2CH·CH_2$	L †	Aq. MeOH	124—125	64
4	I; R = $MeS·CH_2·CH_2$	DL	A *	94—95	53
5	I; R = $Ph·CH_2$	DL	EtOH	146—147	72
6	II; X = Cl, R = H	—	MeOH	250—251 ‡	50
7	II; X = Br, R = H	—	H_2O	232—234 ‡	50
8	II; X = Cl, R = $Ph·CH_2$	DL	MeOH–Et_2O	112—114 §	76
9	II; X = Br, R = $Ph·CH_2$	DL	H_2O	103—104	66

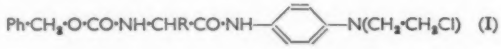
		Found (%)					Required (%)				
No.	Formula	C	H	N	Cl	S	C	H	N	Cl	S
1	$C_{20}H_{23}O_3N_3Cl_2$	56·9	5·4	9·9	16·4	—	56·85	5·4	9·9	16·7	—
2	$C_{21}H_{25}O_3N_3Cl_2$	57·35	5·7	9·6	15·8	—	57·5	5·7	9·6	16·2	—
3	$C_{24}H_{31}O_3N_3Cl_2$	60·0	6·8	8·9	15·2	—	60·0	6·5	8·8	14·8	—
4	$C_{23}H_{29}O_3N_3Cl_2S$	55·7	6·0	8·3	14·6	6·5	55·3	5·8	8·4	14·3	6·4
5	$C_{27}H_{29}O_3N_3Cl_2$	63·1	5·8	8·1	13·3	—	63·0	5·6	8·2	13·8	—
6	$C_{12}H_{17}ON_3Cl_2$,HCl	—	—	12·8	32·6	—	—	—	12·9	32·6	—
7	$C_{12}H_{17}ON_3Cl_2$,HBr	38·0	5·0	—	—	—	38·6	4·85	—	—	—
8	$C_{19}H_{32}ON_3Cl_2$,HCl,MeOH	52·8	6·15	9·5	23·0	—	53·5	6·3	9·4	23·7	—
9	$C_{19}H_{22}ON_3Cl_2$,HBr,$2H_2O$	46·2	5·3	8·4	—	—	45·9	5·6	8·45	—	—

* A, Pentanol–light petroleum. ¶ Colourless or almost colourless rods or needles in each case. † $[\alpha]_D^{20}$ −24·9° ± 1° (*c* 0·92 in MeOH). ‡ With decomp. § Transparent glass; meniscus at 195—200°.

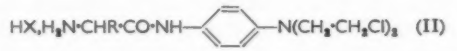
[1] Part V, Bergel and Stock, preceding paper.
[2] Ross, Warwick, and Roberts, *J.*, 1955, 3110.
[3] Hebborn and Danielli, *Nature*, 1956, **177**, 25.
[4] *Idem, Biochemical Pharmacology*, 1958, **1**, 19.
[5] Danielli, *Nature*, 1952, **170**, 863; " Ciba Foundation Symposium on Leukaemia Research," Churchill, London, 1954, p. 263; *Brit. Emp. Cancer Camp. Ann. Rep.*, 1954, **32**, 392; 1956, **34**, 398.
[6] Vaughan, *J. Amer. Chem. Soc.*, 1952, **74**, 6137.
[7] Boissonnas, *Helv. Chim. Acta*, 1951, **34**, 874.

XUM

Removal of the benzyloxycarbonyl group from each of the five compounds was next attempted. Hydrogenolysis of the phenylalanine derivative (I; R = Ph·CH_2) over Adams's platinum oxide catalyst in methanol failed, while hydrogen chloride in glacial acetic acid [8] had little effect in 48 hours at room temperature. However, deacylation by hydrogen chloride in formic acid or hydrogen bromide in glacial acetic acid [9] gave moderate yields of the hydrohalides of the amides (II; X = Cl or Br, R = H or Ph·CH_2). Deacylation of the alanine and leucine intermediates occurred under these conditions; but, although the hydrohalides became solid when rubbed under ether, they were extremely hygroscopic and rapidly became sticky when exposed to air. Attempts to convert the products into, for example, picrates or reineckates were not successful; a solid reineckate {II; X = $[Cr(NH_3)_2(SCN)_4]$, R = Me} of the alanine derivative was prepared but not analytically pure. The methionine compound (I; R = MeS·CH_2·CH_2) yielded, with hydrogen chloride in formic acid, an intractable hygroscopic gum.



(I)



(II)

As pointed out in the introduction it was hoped that the free *N'*-α-aminoacyl-*NN*-di-(2-chloroethyl)phenylenediamines would be broken down *in vivo* to the active *NN*-di-(2-chloroethyl)phenylenediamine. Neither the phenylalanine (CB 3100) nor the glycine (CB 3132) derivative was consistently effective on the Walker carcinoma 256. It appears, therefore, that the tumour tissue cannot split off the α-aminoacyl residue as readily as it does certain acyl radicals such as trichloro- and trifluoro-acetyl.[2]

Experimental

N'-Benzyloxycarbonylaminoacyl-NN-di-(2-chloroethyl)-p-phenylenediamines (I).—The preparation of the glycine derivative illustrates the general method.[6,7] Ethyl chloroformate (0·19 ml., 2 mmol.) was added to an ice-cooled solution of benzyloxycarbonylglycine (418 mg., 2 mmol.) and triethylamine (0·28 mg., 2 mmol.) in dry dioxan (4 ml.). The flask was stoppered and left in ice-water for 10 min. A freshly prepared solution of *NN*-di-(2-chloroethyl)-*p*-phenylenediamine hydrochloride [10] (538 mg., 2 mmol.) and of triethylamine (0·28 ml., 2 mmol.) in dioxan (2 ml.) and water (1 ml.) was then added, and the mixture set aside for 5 min. at room temperature. Addition of water precipitated the anilide which was then crystallised (see Table, No. 1).

In the preparation of the leucine compound (No. 3), chloroform and *iso*butyl chloroformate were used in place of dioxan and ethyl chloroformate.

N'-Aminoacyl-NN-di-(2-chloroethyl)-p-phenylenediamine Hydrohalides (II).—The benzyloxycarbonyl derivatives (I) were best deacylated by the action of hydrogen chloride in formic acid or by hydrogen bromide in glacial acetic acid.[9] Only the glycine and the DL-phenylalanine compound gave crystalline non-deliquescent salts. Two typical experiments are recorded below.

(*a*) *N'*-Benzyloxycarbonylglycyl-*NN*-di-(2-chloroethyl)-*p*-phenylenediamine (I; R = H) (1·69 g.) was dissolved in a saturated solution of hydrogen chloride in 98% formic acid (20 ml.) and left 2 days at room temperature. The solution was evaporated to dryness under reduced pressure, the residual gum treated with water (1 ml.) (to hydrolyse any deliquescent dihydrochloride) which was then evaporated under reduced pressure with gentle warming, and the *glycine anilide hydrochloride* crystallised (No. 6).

(*b*) *N'*-Benzyloxycarbonyl-DL-phenylalanyl-*NN*-di-(2-chloroethyl)-*p*-phenylenediamine (I; R = Ph·CH_2) (650 mg.) was dissolved in an approximately molar solution of hydrogen bromide in glacial acetic acid (8 ml.) and kept for 16 hr. at room temperature. Addition of

[8] Boissonnas and Preitner, *Helv. Chim. Acta*, 1953, **36**, 875.
[9] Ben-Ishai and Berger, *J. Org. Chem.*, 1952, **17**, 1564.
[10] Everett and Ross, *J.*, 1949, 1972.

ether precipitated a gum which became granular when rubbed under water. The *phenylalaninamide hydrobromide* crystallised as the dihydrate (No. 9).

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21. *Co-ordination of Trimethylamine by Halides of Silicon, Germanium, and Tin.*

By J. E. FERGUSSON, D. K. GRANT, R. H. HICKFORD, and C. J. WILKINS.

Trimethylamine reacts with halides of silicon and germanium to give 1 : 1 adducts for which trends in dissociation pressures and heats of formation can be correlated with polar and steric influences. When these are sufficiently favourable, 2 : 1 complexes are also formed. Properties of the 1 : 1 compounds suggest a hexaco-ordinated halogen-bridged structure.

Tetra-*N*-methylethylenediamine forms hexaco-ordinated complexes with silicon and germanium tetrachlorides. Its complex with dichlorodifluorosilane differs from the trimethylamine–chlorofluorosilane adducts in showing no detectable disproportionation.

Trimethylamine and stannic chloride, reacting in the gas phase, give a product of typical composition (amine : halide) 1·35—1·5 : 1. This contains the stable compound $2Me_3N,SnCl_4$ together with a metastable component, probably the 1 : 1 adduct. Residues of composition close to $Me_3N,SnX_4,MeNO_2$ (X = Cl or Br) are obtainable from nitromethane solution.

TRIMETHYLAMINE interacts with halides of Group IV elements [1-6] to form mono- or di-amine adducts, or occasionally both. However, because individual investigations have sometimes related only to specific halides or to restricted reaction conditions the trends in the co-ordination behaviour of the halides have not been clearly established. The present experiments extend to methyltrifluorosilane and the chlorofluorosilanes and include a closer study of the behaviour of germanium and tin halides (Table 1). Reaction of trimethylamine with excess of silicon or germanium halide invariably gives the mono-amine complex. Only when bond polarity and atomic sizes are particularly favourable is a second amine molecule co-ordinated. The same factors would account for trends in dissociation pressures and heats of sublimation of the mono-amine complexes formed by silicon and germanium halides. Pure mono-amine complexes from stannic chloride and bromide could not be isolated. Nevertheless in nitromethane solutions from which residues of composition $Me_3N,SnX_4,MeNO_2$ were obtainable, heats of reaction of the halides with 1 mol. of amine lay in the same order.

[1] Burg, "Fluorine Chemistry," Vol. I, Ed. J. H. Simons, Academic Press Inc., New York, 1950, p. 109.
[2] Burg, *J. Amer. Chem. Soc.*, 1954, **76**, 2674.
[3] Wilkins and Grant, *J.*, 1953, 927.
[4] Barnard, Thesis, Cornell, 1954.
[5] Laubengayer and Smith, *J. Amer. Chem. Soc.*, 1954, **76**, 5935.
[6] Böhme and Boll, *Z. anorg. Chem.*, 1957, **292**, 61.

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The separate effects of polarity and atomic size are illustrated by the varying silane substituents. Thus a predominant steric influence, previously recognised in the chlorosilane series,[2] explains the increasing dissociation pressures on passing from a trihalogenosilane to a methyltrihalogenosilane derivative. Atomic size and bond polarity co-operate in the chlorofluorosilane series, but the former is probably the more important again since

TABLE 1. *Stabilities of mono-amine complexes.*

Compound	Dissn. pres. (mm.)	Heat of subln. (kcal./mole)	Heat of formn. of ion in soln. (kcal./mole)	Compound	Dissn. pres. (mm.)	Heat of subln. (kcal./mole)
Me_3N,SiF_4 [a]	6·5/0° [2]	27·4	—	$Me_3N,SiHF_3$	24/0° [1]	25·1
$Me_3N,SiCl_4$	3·87/ −56·2° [2]	24·0	—	$Me_3N,SiMeF_3$ [c] ...	11·7/ −70·5°	21·2
Me_3N,GeF_4 [a] ...	<0·01/0°	38·4 ± 4	—	$Me_3N,SiHCl_3$ [a] ...	18—23/0° [2]	—
$Me_3N,GeCl_4$ [a] ...	6·4/0°	27·4	18·7 ± 0·6	$Me_3N,SiCl_3F$ [d] ...	*ca.* 260/0°	—
" $Me_3N,SnCl_4$ " [a]	v. small/0°	—	27·6 ± 0·7 [b]	$Me_3N,SiCl_2F_2$ [c, d]	40—70/0°	—
" $Me_3N,SnBr_4$ " [a]	v. small/0°	—	25·7 ± 0·7 [b]	$Me_3N,SiClF_2$ [c, d]	*ca.* 23/0°	—

(*a*) A 2 : 1 complex is formed through uptake of further amine. (*b*) The residues from these solutions were of composition $Me_3N,SnX_4,MeNO_2$, but the heats of mixing of the stannic halides and nitromethane are less than 1 kcal./mole. (*c*) No complex is formed by methyltrichlorosilane down to −95°. (*d*) Disproportionation of these complexes made accurate measurement of physical properties impossible.

the polarity of the silicon–fluorine bond is much reduced through π-bonding.[7] On the other hand polarity must determine the relative behaviour of silcon tetrachloride and methyltrichlorosilane since the substituents are now of closely similar size.[8] The absence of interaction between monosilane and trimethylamine [2] or between certain substituted silanes and pyridine or *p*-toluidine [9] is consistent with the sensitivity of the co-ordination behaviour of a silicon centre to these influences.

The wide occurrence of the mono-amine complexes and the regular trends in their dissociation pressures suggest that the crystalline compounds conform to a common structural type within which lattice energies and entropies of formation do not vary greatly. The suggestion of a covalency of five for the central (silicon) atom [10] is questionable. The (almost) complete dissociation in the vapour state of the complexes formed by silicon tetrafluoride,[3] germanium tetrachloride,[4] and dichlorosilane [2] suggests that the crystalline compounds are not unimolecular; no other examples of five-fold co-ordination around silicon and germanium are known. Four-fold co-ordination arising from ionisation [11] or six-fold co-ordination through halogen-bridging [12] are both alternatives which would account for the conspicuous effect on amine co-ordination of the first halogen atom introduced into the silane molecule. Other lines of evidence, though not individually decisive, are most readily interpreted in terms of the latter constitution. Stannic chloride and bromide, for which ionisation should occur readily, are exceptional in not forming pure stable mono-amine adducts. The specific conductivity of molten Me_3N,SiF_4 is only $1{\cdot}4 \times 10^{-3}$ ohm^{-1} cm.$^{-1}$ and for $Me_3N,GeCl_4$ in acetonitrile $\Lambda_{0\cdot0075} = 31$ as compared with $\Lambda_{0\cdot018} \simeq 390$ for the ionic compound Me_3N,SiH_3I.[11] In its low volatility the iodosilane adduct differs so sharply from comparable members of the self-consistent series of tetrahalide and chlorosilane complexes as to suggest a different constitution. It is significant that of the silicon–halogen bonds that with iodine is the most readily ionised.[13]

Formation of hexaco-ordinated complexes from silicon and germanium tetrachlorides

[7] Curran, Witucki, and McCusker, *J. Amer. Chem. Soc.*, 1950, **72**, 4471.
[8] Hückel, " Structural Chemistry of Inorganic Compounds," Vol. I, Elsevier Publishing Co., 1950, p. 170.
[9] Eaborn, *J.*, 1955, 2047.
[10] Stone and Seyferth, *J. Inorg. Nuclear Chem.*, 1956, **2**, 325.
[11] Aylett, Emeléus, and Maddock, *ibid.*, 1955, **1**, 187.
[12] As, *e.g.*, the structure of the ion AlF_5^{2-}; Brossett, *Z. anorg. Chem.*, 1937, **235**, 139.
[13] Eaborn, *J.*, 1950, 3077.

occurs with tetra-*N*-methylethylenediamine. That this ligand occupies two co-ordination positions is shown by the low dissociation pressures of its (1 : 1) adducts compared with those from trimethylamine, to which its individual amino-groups would have similar basic and steric properties. The conductivity of the silicon compound (which alone is soluble) in benzene is negligible. The compound * from tetra-*N*-methylethylenediamine and dichlorodifluorosilane differs from the trimethylamine–chlorofluorosilane adducts in showing no evidence from drifting dissociation pressure of spontaneous rearrangement of halogen atoms. This may be significant because a bridged structure, which is possible only in complexes from the unidentate amine, would provide a reaction path of low activation energy.

The steric requirement of trimethylamine lies between those of pyridine and of triethylamine which have (along with tributylamine) been reported by Trost [14] to form **4 : 1** complexes with tetrachlorides. The ready formation of dipyridine adducts by silicon tetrahalides [15,16] is consistent with the low steric demand of this base, but any predominantly steric interpretation of amine behaviour would be incompatible with Trost's results. However, re-examination of the interaction of silicon tetrachloride and triethylamine failed to substantiate the formation of a complex. The very small amount of solid obtained gave an *X*-ray powder photograph identical with that from triethylamine hydrochloride. The formation of tetrapyridinesilicon tetrachloride has also been discounted [16] and the existence of other such silicon tetrachloride adducts must be questioned.

Experimental

Procedures were based on vacuum technique. Compound formation was examined at temperatures to −78° by determining pressure–composition isotherms and by quantitative synthesis (Table 2). The purity of all reactants was checked tensimetrically. Germanium tetrafluoride from barium fluorogermanate [17] was difficult to purify but vapour pressures of the final sample agreed closely with those given by Fischer and Weidemann.[18]

Calorimetric measurements were made as described by Brown and Horowitz,[19] excepting that, to avoid use of mercury, the solutions were brought together by rupturing a glass membrane across the lower end of the calorimeter partition. Rigorous precautions were taken against access of moisture. Standard solutions of trimethylamine in nitromethane were made by breaking a weighed ampoule beneath the solvent and were checked by titration.

Table 2. *Characterisation of addition complexes.*

Compound	Combining ratio (obs.)	M.p.; thermal stability	Dissn. pres., $\log_{10} p$
$Me_3N,SiMeF_3$	0·99 : 1	−51·5° [b]	12·745 − 2319/T
Me_3N,GeF_4	1·03 : 1	129—131 (decomp.) [d]	12·188 − 4315/T [d]
$2Me_3N,GeF_4$	2·00 : 1 [a]	Decomp. at 120°	—
$Me_3N,GeCl_4$	0·98 : 1	75—76°	11·764 − 2995/T
$2Me_3N,GeCl_4$	2·01 : 1	Not formed at −60° [c]	—
$2Me_3N,SnCl_4$	1·99 : 1	174—175° (decomp.)	—

(*a*) Deduced from isotherm at 0°. (*b*) The dissociation pressure reaches twice the vapour pressure of trimethylamine at −53°. (*c*) Sublimes incongruently at −78°. (*d*) Near 100° there is slight formation of uncondensable gas. Dissociation pressures were: 64°, 0·25 mm.; 74·1°, 0·60; 84·3°, 1·25; 94·0°, 2·74; 96·5°, 3·07.

Behaviour of Chlorofluorosilanes towards Trimethylamine.—Mono-amine adducts were obtained in each case by passing the mixed vapours through a trap at −78° irrespective of the component in excess,[3] but on allowing $Me_3N,SiCl_2F_2$ and $Me_3N,SiClF_3$ to remain in contact with

* The desirability of examining this compound was suggested by a Referee.

[14] Trost, *Canad. J. Chem.*, 1951, **29**, 1075; 1952, **30**, 835.
[15] Schwarz and Wannagat, *Z. anorg. Chem.*, 1954, **277**, 73.
[16] Wannagat and Vielberg, *ibid.*, 1957, **291**, 310.
[17] Dennis and Laubengayer, *Z. phys. Chem.*, 1927, **130**, 520.
[18] Fischer and Weidemann, *Z. anorg. Chem.*, 1933, **213**, 106.
[19] Brown and Horowitz, *J. Amer. Chem. Soc.*, 1955, **77**, 1730.

XUM

excess of amine at this temperature conversion into the di-amine complexes occurred during 8—24 hr. Table 3 gives typical compositions. Isotherms having sharp breaks could not be obtained for trichlorofluorosilane and dichlorodifluorosilane owing to disproportionation, which likewise caused the divergence of the compositions of the dichlorodifluorosilane adducts from the stoicheiometric ratios.

TABLE 3.

Silane	$SiCl_3F$	$SiCl_2F_2$	$SiClF_3$
Amine : silane in solid condensed from gaseous reactants at −78°	1·02	0·95—1·05	0·995
Amine : silane after standing with excess of liquid amine at −78°	1·02	1·92	1·96

At 0° the initial dissociation pressure of $Me_3N,SiCl_3F$ fell and that of $Me_3N,SiCl_2F_2$ rose too quickly to permit reproducible measurements. Disproportionation of the former was almost quantitative after 4 months at ordinary temperature. From 39·5 ml. of trichlorofluorosilane and 19·7 ml. of amine in a sealed tube there were recovered 28·4 ml. of silicon tetrachloride (calc., 29·6 ml.) and crystalline $2Me_3N,SiF_4$ (vap. pres. 6 mm./0°) which released 8·3 ml. of amine (calc., 9·85 ml.) upon distillation through a trap at −78°.[3]

Stannic Chloride and Trimethylamine.—After 171·6 ml. of amine and 41·0 ml. of stannic chloride were allowed to react for 24 hr. at −10°, 90·8 ml. of amine were recovered, corresponding to a residue of composition 1·97 : 1. Absorption of amine occurred rapidly up to the equimolecular ratio and thereafter more slowly, indicating intermediate formation of a phase of this composition. The *X*-ray powder photograph was identical with that from a product of composition 1·96 : 1 obtained from excess of stannic chloride at room temperature, θ values for Cu-K_α radiation being: 6·6°(s), 7·0°(s), 7·3°(m), 8·0°(s), 8·3°(s), 9·1°(w), 10·9°(m), 11·6°(w), 12·4°(m), 13·4°(m), 14·3°(w), 14·7°(w), 16·4°(m), 16·9°(m), 18·0°(m), 18·4°(m), 18·8°(w), 19·4°(m), 19·9°(m), 21·2°(s), 22·3°(m), 22·8°(m), 23·9°(s), 24·9°(m).

Contact with either liquid component was necessary to promote formation of the stable 2 : 1 phase, presumably because the initial crystalline phase is metastable and disproportionates in contact with solvent. Contrary to Laubengayer and Smith [5] who report the 2 : 1 compound from gaseous reactants, combination of the vapours carried in nitrogen repeatedly gave products of typical composition 1·35—1·5 : 1 irrespective of the component in excess. These samples gave the stronger *X*-ray powder lines of the 2 : 1 phase together with lines, probably corresponding to a 1 : 1 phase, at 6·2°(s), 10·3°(m), 12·1°(m), 14·6°(m), 15·1°(w), 19·2°(m).

When 145·4 ml. of stannic chloride and 146·3 ml. of amine were distilled into nitromethane and the volatile material pumped off at room temperature, 4·0 ml. of halide were removed with the solvent so that the combining ratio amine : halide was 1·035 : 1. Traces of solvent free from halide continued to distil during 16 hr. leaving 2·34 g. of white solid (Found: C, 12·4; H, 3·4; N, 6·6; Cl, 38·2. Calc. for $Me_3N,SnCl_4,MeNO_2$: C, 12·6; H, 3·15; N, 7·4; Cl, 37·3. Calc. for $Me_3N,SnCl_4$: C, 11·3; H, 2·8; N, 4·4; Cl, 44·4%). The *X*-ray powder photograph was distinctive but included weak lines corresponding to several of the stronger lines of $2Me_3N,SnCl_4$. It is concluded that 3—4% of this phase was present.

Stannic bromide (1·008 g.) and trimethylamine in equimolecular proportion in nitromethane gave a *residue* (1·271 g.) (Found: C, 9·2; H, 2·4; N, 4·4; Br, 57·3. $Me_3N,SnBr_4,MeNO_2$ requires C, 8·6; H, 2·2; N, 5·0; Br, 57·2%).

Co-ordination of Tetra-N-methylethylenediamine.—Addition of amine [20] (b. p. 121—122°) to silicon tetrachloride or germanium tetrachloride at room temperature caused a sharp fall in pressure at the equimolecular ratio. No other breaks in the isotherms were detected. The adducts were also prepared by using light petroleum (low-boiling) as diluent. Compositions of samples of silicon derivative always corresponded to an amine : halide ratio of 1·03—1·06 : 1, probably because incongruent sublimation led to preferential loss of silicon tetrachloride under vacuum. The *germanium derivative* had C, 22·5; H, 4·55; N, 8·5; Cl, 42·2 ($C_6H_{16}N_2GeCl_4$ requires C, 21·8; H, 4·9; N, 8·5; Cl, 42·9%). Dissociation pressures of the former are 2 mm. at 0°, 6 mm. at 18°, and of the latter <0·1 mm. at 0°. The silicon derivative immediately hydrolyses in air. Both are insoluble in acetonitrile, dimethylformamide, nitromethane, and triethylamine.

During 14 days the dissociation pressure (<0·1 mm. at 20°) of the dichlorodifluorosilane adduct (combining ratio 1·01 : 1) did not increase as would have been expected if rearrangement to yield the silicon tetrachloride adduct had occurred. However, treatment with hydrogen

[20] Hanhart and Ingold, *J.*, 1927, 997.

chloride seemingly caused rearrangement because the silane which was slowly released contained a full range of disproportionation products, as judged from rough examination of vapour pressures of fractions.

Triethylamine and Silicon Tetrachloride.—In a typical experiment made in the vacuum system 5·5 g. of chloride and 23·1 g. of amine (redistilled and dried over sodium) gave 0·31 g. of triethylamine hydrochloride. This was identified from its *X*-ray powder photograph since $4Et_3N,SiCl_4$ would be close in composition. It was not possible to eliminate formation of this product through repurification of the reactants.

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22. *Kinetic Salt Effects and Mechanism in the Hydrolysis of Positively Charged Esters.*

By G. AKSNES and J. E. PRUE.

A kinetic study of the acid and alkaline hydrolysis of four esters containing a quaternary ammonium group is reported. Analysis of the dependence of the specific salt effects and the rate constants on the distance between the reaction centre and the positively-charged nitrogen atom gives information about the origin of the specific salt effects and the mechanism of ester hydrolysis. It is concluded that in acid-catalysed hydrolysis the proton is attached to the carbonyl oxygen atom of the ester group.

AN investigation [1] of the rates of alkaline hydrolysis of half-esters of dicarboxylic acids showed that with alkali-metal salts there is a negative specific salt effect whose magnitude depends on the separation of the charge of the ester ion from the reaction centre. It was therefore of interest to see whether a similar phenomenon exists in both the acid and alkaline hydrolysis of a series of esters carrying a positively-charged quaternary ammonium group. This was particularly so since Butterworth, Eley, and Stone's results [2] for the acid-catalysed hydrolysis of acetylcholine ($Me_3\overset{+}{N}\cdot[CH_2]_2\cdot O\cdot COMe$) bromide do not show the expected primary kinetic salt effect for a reaction between two positively charged ions; on the other hand, Bell and Lindars's results [3] for the ester-ion $Et_3\overset{+}{N}\cdot CH_2\cdot CO_2Et$ show normal salt effects for both acid and alkaline hydrolysis. Furthermore, we shall show that our results provide additional information on the detailed mechanism of hydrolysis of esters.

EXPERIMENTAL

2-Methoxycarbonylethyltrimethylammonium Bromide, $(Me_3\overset{+}{N}\cdot[CH_2]_2\cdot CO_2Me)Br^-$.—Ethylene chlorohydrin was converted into β-bromopropionic acid by successive treatment with sodium cyanide and 48% hydrobromic acid.[4] The acid was converted (70% yield) into the methyl ester (b. p. 62°/12 mm.) by treatment with methyl alcohol in carbon tetrachloride, toluene-*p*-sulphonic acid being used as catalyst. Excess of dry trimethylamine was added to a 30% solution of the ester in alcohol at 0°, and the mixture kept overnight; the yield of quaternary salt was almost quantitative. The *salt*, precipitated with ether and recrystallised from alcohol, had m. p. 182° (Found: Br, 35·27. $C_7H_{16}O_2NBr$ requires Br, 35·34%).

3-Methoxycarbonylpropyltrimethylammonium Bromide, $(Me_3\overset{+}{N}[CH_2]_3\cdot CO_2Me)Br^-$.—Propane-1 : 3-diol was converted into 3-chloropropan-1-ol by treatment with hydrogen chloride.[5]

[1] Hoppé and Prue, *J.*, 1957, 1775.
[2] Butterworth, Eley, and Stone, *Biochem. J.*, 1953, **53**, 30.
[3] Bell and Lindars, *J.*, 1954, 4601.
[4] "Organic Syntheses," John Wiley and Sons, New York, 1946, Vol. I, pp. 131, 256.
[5] *Op. cit.*, p. 533.

XUM

Potassium cyanide (34 g.) was added to a stirred solution of 3-chloropropan-1-ol (40 g.) in 200 ml. of ethanol–water (3 : 1 v/v). The solution was then boiled for 1½ hr., cooled, and filtered, and the alcohol and water were distilled off under reduced pressure to obtain 3-cyanopropan-1-ol (30 g., b. p. 122°/15 mm.). This was converted into γ-bromobutyric acid (m. p. 32°) by treatment with hydrobromic acid, and the methyl ester (b. p. 79°/20 mm.) prepared by treatment of the acid with excess of methyl alcohol, sulphuric acid being used as catalyst. A 20% yield of the quaternary salt was obtained by heating the ester with excess of alcoholic trimethylamine (33%) in a sealed tube at 70° for 20 hr. After the solution had cooled, the *salt* was precipitated with dry ether and recrystallised from acetone. It had m. p. 82° (Found: Br, 33·15; OMe, 12·88. $C_8H_{16}O_2NBr$ requires Br, 33·28; OMe, 12·92%).

2-*Acetoxyethyltrimethylammonium Bromide* (*Acetylcholine Bromide*), $(Me_3N{\cdot}[CH_2]_2{\cdot}O{\cdot}COMe)^+Br^-$.—A commercial sample (B.D.H. Ltd.), recrystallised from alcohol, had m. p. 146° (Found: Br, 35·25; $MeCO_2^-$, 26·08. Calc. for $C_7H_{16}O_2NBr$: Br, 35·34; $MeCO_2^-$, 26·11%).

3-*Acetoxypropyltrimethylammonium Iodide*, $(Me_3N{\cdot}[CH_2]_3{\cdot}O{\cdot}COMe)^+I^-$.—Excess of alcoholic trimethylamine (10 g., 33%) was added to 3-chloropropyl acetate (7 g.) and the mixture kept in a sealed tube at 110° for 16 hr. The chloride, obtained by precipitation with ether after cooling the alcoholic solution to −50°, was extremely hygroscopic. It was therefore converted into the less hygroscopic iodide by dissolving it in acetone, adding excess of sodium iodide to precipitate sodium chloride which was filtered off, and then distilling off the acetone. The *iodide*, recrystallised three times from alcohol–ether, had m. p. 80° (Found: $MeCO_2^-$, 20·46. $C_8H_{18}O_2NI$ requires $MeCO_2^-$, 20·56%).

Kinetic Measurements.—The rates of hydrolysis of the quaternary esters were studied in solutions of hydrochloric acid and sodium hydroxide at 25° ± 0·01°. Carbonate-free sodium hydroxide solution was prepared by dilution of a concentrated stock solution. All solutions were standardised against " AnalaR " potassium hydrogen phthalate.

TABLE 1.

(k_H in sec.$^{-1}$ l. mole^{-1} and concentrations in mole l.$^{-1}$.)

	2-Acetoxyethyltrimethylammonium bromide				3-Acetoxypropyltrimethylammonium bromide			
10^3[HCl]	96·71	70·85	51·59	25·80	78·54	58·89	46·37	27·45
10^3[ester] ...	33·79	23·05	26·61	28·94	25·06	25·21	24·83	23·55
10^5k_H(exp.) ...	2·82	2·68	2·62	2·47	5·10	5·03	5·00	4·83
10^5k_H(calc.) ...	2·82	2·68	2·60	2·47	5·08	5·05	4·98	4·85

	3-Methoxycarbonylpropyltrimethylammonium bromide			2-Methoxycarbonylethyltrimethylammonium bromide		
10^3[HCl]	78·54	58·34	46·37	10^3[HCl]	74·76	27·45
10^3[ester]	28·56	41·36	26·23	10^3[ester]	33·04	27·15
10^5k_H(exp.) ...	2·08	2·05	1·95	10^4k_H(exp.) ...	7·33	6·65
10^5k_H(calc.) ...	2·07	2·05	1·95	10^4k_H(calc.).....	7·33	6·65

The reactions in acid were slow ($t_{\frac{1}{2}}$ = 70—500 hr.) and for each concentration of acid several solutions were made up in 100 ml. standard flasks, each containing an accurately weighed amount of ester. The solutions were left for varying times corresponding to 20—60% hydrolysis, and the contents then weight-titrated against standard barium hydroxide solution. The solutions were well shaken during titration to avoid local temporary excesses of hydroxyl ions which would cause further ester hydrolysis. The first-order rate constants obtained did not deviate by more than 1% from their mean value. The mean values of the corresponding second-order rate constants k_H for reaction between the ester and hydrogen ion are given in Table 1.

The reactions in alkali were much faster ($t_{\frac{1}{2}}$ = 1—6 min.). A weighed amount of ester was dissolved in an equivalent amount of standard sodium hydroxide solution in a conical flask previously placed in the thermostat; the esters dissolved almost instantaneously. After a suitable time excess of hydrochloric acid was added and the solution back-titrated against barium hydroxide solution. The individual values of the second-order rate constants k_{OH} did not deviate by more than 2% from the mean values recorded in Table 2. The ionic strength decreases during the alkaline hydrolysis of 3-methoxycarbonylpropyltrimethylammonium bromide, and the results in Table 2 for this ester are the average of several determinations at

XUM

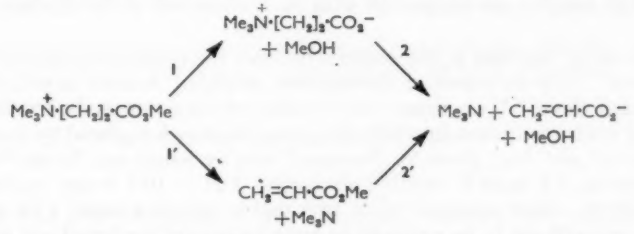
each concentration in which the reaction was stopped at approximately 50% hydrolysis; in analysing the results the ionic strength was taken as the value at 25% hydrolysis.

TABLE 2.

(k_{OH} in sec.$^{-1}$ l. mole^{-1} and concentrations in mole l.$^{-1}$.)

	3-Acetoxytrimethylammonium iodide				3-Methoxycarbonylpropyltrimethylammonium bromide				
10^3[NaOH]	34·68	23·12	17·34	11·56	34·68	23·12	19·87	17·34	11·56
$10k_{OH}$(exp.)	4·35	4·60	4·70	5·05	4·90	5·15	5·40	5·46	5·70
$10k_{OH}$(calc.)	4·35	4·60	4·76	5·01	4·90	5·21	5·33	5·43	5·71

The alkaline hydrolysis of the acetylcholine ion was too fast for accurate study, whilst that of the 2-methoxycarbonylethyltrimethylammonium ion is not a simple reaction. Willstätter [6] found previously that in addition to propylbetaine, trimethylamine and the acrylate ion are also produced. These could result from the attack of the hydroxyl ion on propylbetaine, and we find that on complete hydrolysis a quantitative yield is obtained of trimethylamine and acrylate ion. However, a considerable amount of methyl acrylate is formed as an intermediate, and can be extracted with carbon tetrachloride. The formation of methyl acrylate shows that there are two alternative reaction paths, a hydroxyl ion being consumed at each stage:



Semiquantitative studies show that the rate constants of 1 and 1′ are comparable and about 2—10 sec.$^{-1}$ l. mol.$^{-1}$ at 25°. Reaction 2 is approximately 1000 times slower than 1′, which is reasonable, because the negative charge on the carboxylate ion will strongly reduce the readiness of the β-hydrogen atom to be removed as a proton.

DISCUSSION

Salt effects due to the addition of alkali-metal salts can be adequately described [1] by the equation

$$\log k = \log k^\circ + \frac{2z_A z_B A I^{\frac{1}{2}}}{1 + I^{\frac{1}{2}}} + BI \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where z_A and z_B are the charges on the reacting ions, I is the ionic strength, A is a constant of the Debye–Hückel theory with the value 0·509 (l. mole^{-1})$^{\frac{1}{2}}$ for water at 25°, and B is an empirical parameter which takes account of any specific salt effects. We use this equation in this work. The values of k° and B can be found by plotting $\log k - 2z_A z_B A I^{\frac{1}{2}}/(1 + I^{\frac{1}{2}})$ against I, and are given in Table 3. The values of k (calc.) in Tables 1 and 2 are obtained by inserting these values of k° and B in eqn. (1), and we see that the calculated and observed values of k agree closely. This method of analysing the data is especially suitable if accurate values of k° are required. We now consider what further conclusions we can draw from the values of B and k°; we have numbered the esters in Table 3 for ease of reference.

The acid hydrolysis of ester 3 shows the expected positive salt effect, the rate constant increasing from $k_H = 1{\cdot}64 \times 10^{-5}$ sec.$^{-1}$ l. mole^{-1} at $I = 0$ (Table 3) to $2{\cdot}82 \times 10^{-5}$ at $I = 0{\cdot}13$ in contrast to Butterworth, Eley, and Stone's result,[2] $k_H = 3 \times 10^{-5}$. The specific salt effects are negative for acid hydrolysis, positive for alkaline hydrolysis, and tend to increase as the distance increases between the positively-charged quaternary nitrogen

atom and the reaction centre. This is in agreement with the explanation previously advanced for such specific effects.[1] As the distance between the charges in the activated complex increases, the more each charge tends to build up its own ion atmosphere. This leads to a reduction in the normal positive salt effect for a reaction between two ions of

TABLE 3.

($k°$ in sec.$^{-1}$ l. mole^{-1}, B in l. mole^{-1}, r in Å.)

	Acid hydrolysis				Alkaline hydrolysis			
	$-B$	$10^5 k_H°$	α	r	B	$k_{OH}°$	α	r
1. $Me_3\overset{+}{N}\cdot CH_2\cdot CH_2\cdot CO_2Me$	$0{\cdot}3_2$	0·44	27·2	2·2	—	—	—	—
2. $Me_3\overset{+}{N}\cdot CH_2\cdot CH_2\cdot CH_2\cdot CO_2Me$...	$0{\cdot}2_6$	1·24	5·7	4·1	$0{\cdot}1_8$	0·76	0·133	3·5
3. $Me_3\overset{+}{N}\cdot CH_2\cdot CH_2\cdot O\cdot COMe$	$0{\cdot}2_6$	1·64	6·7	3·8	—	~1·8	0·061	2·5
4. $Me_3\overset{+}{N}\cdot CH_2\cdot CH_2\cdot CH_2\cdot O\cdot COMe$	$0{\cdot}7_5$	3·43	3·3	6·0	$0{\cdot}3_8$	0·67	0·130	3·5

the same charge, and in the normal negative salt effect for a reaction between two oppositely charged ions. The values of B and their dependence on the charge separation in the activated complex are comparable with those observed [1] in the alkaline hydrolysis of half-esters.

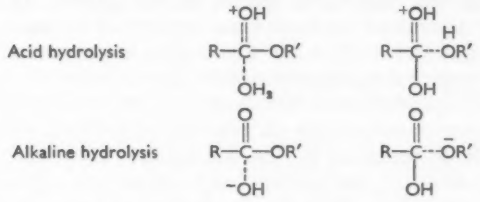
The values of $k_H°$ increase as the distance between the positive charge and the reaction centre increases. This we expect on electrostatic grounds. A more quantitative analysis can be made as follows. We compare the $k°$ values of the esters studied with those of the corresponding uncharged esters in which the group Me_3N^+– is replaced by hydrogen. We use values of $k_H°$ and $k_{OH}°$ given by Palomaa [7] and by Salmi and Leimu [8] respectively. They are (units sec.$^{-1}$ l. mole^{-1}): methyl propionate, $1{\cdot}21 \times 10^{-4}$, 0·164; methyl butyrate, $7{\cdot}05 \times 10^{-5}$, 0·101; ethyl acetate, $1{\cdot}10 \times 10^{-4}$, 0·110; propyl acetate, $1{\cdot}13 \times 10^{-4}$, 0·087. These values are unlikely to be seriously in error because of neglected salt effects, as the reactions are between an ion and a neutral molecule. The values of α in Table 3 are the quotient $k°$(neutral)/$k°$(charged). If we ascribe the differences of α from unity entirely to the electrostatic interaction between the charges in the activated complex, α is given by [9,10,11] $\ln \alpha = z_A z_B e^2/DkTr$ where e is the electronic charge, D the dielectric constant of the medium, k Boltzmann's constant, T the absolute temperature, and r the distance between the charges. Setting $D = 78{\cdot}5$, we obtain the values of r recorded in Table 3. The absolute values of r are too small, and in the acid hydrolysis the increments of r as the chain is lengthened are rather large. This is probably due to using the dielectric constant of the solvent rather than some smaller value; a similar effect is found in interpreting the dependence on chain length of the ratio of the acidity constants of dicarboxylic acids.[11]

The values of r fall into three groups, *viz.*, 1(H^+), 3(OH^-); 2(H^+), 3(H^+), 2(OH^-), 4(OH^-); 4(H^+). We can only explain the similar values of r for acid hydrolysis of esters 2 and 3 if in the activated complex for acid hydrolysis the proton and positive charge are on the carbonyl oxygen and not on the ether oxygen atom. Furthermore, if in alkaline hydrolysis the negative charge in the activated complex is shared between the attacking hydroxyl ion and the ether oxygen, we see why the r values for alkaline hydrolysis of esters 2 and 4 are the same and similar to those for acid hydrolysis of esters 2 and 3, for the distance between the charge on the quaternary nitrogen atom and the centroid of charge on the ester end of the molecule will be similar in all four cases. That the values of r for alkaline hydrolysis are slightly less may be due to some coiling of the chain when it has oppositely-charged ends. Just as the r values for acid hydrolysis of 2 [2(H^+)] and

[6] Willstätter, *Ber.*, 1902, **35**, 584.
[7] Palomaa, *Ber.*, 1938, **71**, *B*, 480.
[8] Salmi and Leimu, *Suomen Kem.*, 1947, **20**, *B*, 43.
[9] Bjerrum, *Z. phys. Chem.*, 1923, **106**, 219.
[10] Ingold, *J.*, 1931, 2170.
[11] Wheland, "Advanced Organic Chemistry," John Wiley and Sons, New York, 1949, p. 434.

alkaline hydrolysis of 4 [4(OH^-)] are similar so are those for acid hydrolysis of 1 and alkaline hydrolysis of 3.

The most recent work [12] on the mechanism of ester hydrolysis, including the study of isotopic oxygen exchange, suggests that a symmetrical intermediate complex is formed in a reaction involving the solvent. This is probably the monoester of the ortho-acid $R{\cdot}C(OH)_2{\cdot}OR'$. The existence of catalysis by hydrogen or hydroxyl ions indicates that formation of the monoester, and conversion into the acid or reversion into the ester, takes place most readily through activated complexes having the composition of the protonated or deprotonated ortho-ester. Our observations are consistent with the two activated complexes' in each case having the following approximate charge distributions:



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THE UNIVERSITY, READING. [*Received, July 2nd,* 1958.]

[12] Bender, Ginger, and Unik, *J. Amer. Chem. Soc.*, 1958, **80**, 1044.

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23. *Kinetic Salt Effects in the Reaction between Persulphate and Iodide Ions.*

By A. INDELLI and J. E. PRUE.

The second-order reaction between persulphate and iodide ions can be accurately and conveniently studied in dilute solution by using a polarised electrode to determine the times of reappearance of iodine after the injection of successive quantities of sodium thiosulphate. The kinetic salt effects of a variety of added salts of various valency types have been studied. Over a range of ionic strengths above 0·0034 mole $l.^{-1}$ the effects are very specific; there is some correlation with the concentration of ions of charge opposite to that of the reactants, but none with the ionic strength. The effects cannot be satisfactorily interpreted with Debye–Hückel-type equations for the activity coefficients of the reactant ions and the activated complex, even with the additional assumption of ion association. The theory of kinetic salt effects is discussed.

IN 1949 Olson and Simonson,[1] discussing the effect of addition of inert salts on the rates of ionic reactions, asserted that for reactions between ions of like charge the effect is almost exclusively due to the concentration and character of ions of charge opposite to that of reactants, and that the rate is not simply dependent on the ionic strength of the solutions. Kilpatrick [2] pointed out that in Brönsted's original formulation [3] of the theory of kinetic salt effects, before the advent of the Debye-Hückel theory,[4] the importance of specific interactions between ions of opposite charge was clearly recognised. There can be little doubt that the fundamental equation of Brönsted's theory of kinetic salt effects is correct, *viz.*, for reaction between two ions of charges z_A and z_B respectively, $k = k^\circ f_A f_B / f_{AB}$ where

[1] Olson and Simonson, *J. Chem. Phys.*, 1949, **17**, 1167.
[2] Kilpatrick, *Ann. Rev. Phys. Chem.*, 1951, **2**, 255.
[3] Brönsted, *Z. phys. Chem.*, 1922, **102**, 169.

k° is a constant for the solvent and f_A, f_B, and f_{AB} are activity coefficients which tend to unity as the total concentration of ions in solution tends to zero; f_{AB} is the activity coefficient of the activated complex, and Brönsted's theory can be regarded [5] as a special application of the transition-state theory of reaction kinetics. Brönsted [3] tested the equation with experimental results for the activity-coefficient factor derived from solubility measurements. Barrett and Baxendale [6] recently showed that at sufficiently low ionic strengths ($<4 \times 10^{-3}$ mole l.$^{-1}$) the variation with ionic strength of the rate constant of a reaction between two ions of opposite charge, *viz.*, $Fe^{2+} + Co(C_2O_4)_3^{3-}$, is close to that predicted by substituting the Debye–Hückel limiting-law values for the activity coefficients in the Brönsted equation; the correlation of the rate constant with ionic strength is good, and only small specific effects appear. In other cases, results can be quantitatively described [7] up to an ionic strength of 0·1 mole l.$^{-1}$ by the equation $\log k = \log k^\circ + 2z_Az_BAI^{\frac{1}{2}}/(1 + I^{\frac{1}{2}}) + BI$ where A is a constant of the Debye–Hückel theory and B is an empirical parameter which takes account of small specific effects. However, the repeated reproduction in text-books of a diagram published by Livingston [8] in 1930, in which the rate constants for six reactions of different charge types are shown to vary approximately as predicted by the limiting-law, even when the ionic strengths increase to 0·04—0·07 mole l.$^{-1}$, has perhaps led to an attitude which underestimates the specific effects which can occur. Data for the reaction between bromoacetate and thiosulphate ions were used in Livingston's diagram, but when bivalent cations are present as well as alkali-metal cations large specific effects arise [9] which have been quantitatively interpreted [10] in terms of ion association. Olson and Simonson [1] concluded that, even for univalent cations, the cation concentration was more significant than the ionic strength. Scatchard [11] has discussed the effects observed for this reaction and concludes that they are in accord with Mayer's treatment [12] of electrolyte solutions.

A reaction of the same charge type is that between persulphate and iodide ions to produce iodine and sulphate ions. It is of the first order with respect to both reactants and King and Jacobs [13] and King and Knudsen [14] obtained results that followed the limiting-law prediction up to an ionic strength of 0·025 mole l.$^{-1}$; Soper and Williams [15] found a greater increase of rate constant with increasing ionic strength than predicted by the limiting law. In most of these experiments the ionic strength was varied by changing the reactant concentrations. Specific salt effects have been observed at much higher concentrations by Howells,[16] Rolla and Carassiti,[17] and Carassiti and Dejak,[18] who interpreted the results in terms of a theory due to Bonino.[19] We have found that accurate results for this reaction can conveniently be obtained in dilute solution by using a polarised electrode [20] to determine the times of reappearance of iodine in the solution after the injection of successive small quantities of sodium thiosulphate solution with a microsyringe. In this way we have studied the kinetic salt effects of a variety of added salts of various valency types. Large specific effects were observed and it is not possible to

[4] Debye and Hückel, *Physik. Z.*, 1923, **24**, 185.
[5] Eyring and Wynne-Jones, *J. Chem. Phys.*, 1935, **3**, 492.
[6] Barrett and Baxendale, *Trans. Faraday Soc.*, 1956, **52**, 210.
[7] Guggenheim and Prue, " Physicochemical Calculations," North-Holland Publishing Co., Amsterdam, 1956, p. 466.
[8] Livingston, *J. Chem. Educ.*, 1930, **7**, 2899.
[9] LaMer and Fessenden, *J. Amer. Chem. Soc.*, 1932, **54**, 2351.
[10] Wyatt and Davies, *Trans. Faraday Soc.*, 1949, **45**, 774; Davies and Williams, *ibid.*, 1958, **54**, 1547.
[11] Scatchard, " Electrochemical Constants," National Bureau of Standards Circular 524, 1953, p. 185.
[12] Mayer, *J. Chem. Phys.*, 1950, **18**, 1426.
[13] King and Jacobs, *J. Amer. Chem. Soc.*, 1931, **53**, 1704.
[14] King and Knudsen, *J. Amer. Chem. Soc.*, 1938, **60**, 687.
[15] Soper and Williams, *Proc. Roy. Soc.*, 1933, *A*, **140**, 59.
[16] Howells, *J.*, 1939, 463; 1941, 641; 1946, 203.
[17] Rolla and Carassiti, *Boll. Fac. Chim. Ind., Bologna*, 1949, **7**, 37.
[18] Carassiti and Dejak, *Atti. Accad. Sci. Inst. Bologna*, 1955, **11**, 1.
[19] Bonino, *Mem. R. Accad. ital.*, 1933, **4**, 415.
[20] Sully, *Chem. and Ind.*, 1955, 1146.

describe the results over the ionic strength range 0·004—0·1 mole l.$^{-1}$ in terms of Debye–Hückel-type equations for the activity coefficients. There is some correlation of the rate constants with the concentration and character of ions of charge opposite to that of the reactants.

Experimental

Materials.—" AnalaR " reagents were used, except for sodium tri- and tetra-metaphosphates ($Na_3P_3O_9$ and $Na_4P_4O_{12}$), prepared and purified as described elsewhere,[21, 22] and sodium iodide, lithium and lanthanum chlorides, potassium perchlorate, tetramethyl- and tetraethylammonium bromide, and hexamminocobalt trichloride which were B.D.H. laboratory reagents. All solutions were prepared with water of conductivity less than 10^{-6} ohm^{-1} cm.$^{-1}$ from an ion-exchange column. Potassium iodide and sodium thiosulphate solutions were standardised against " AnalaR " potassium iodate. Potassium persulphate solution was standardised by adding a sample to a large excess of potassium iodide and a trace of ferrous sulphate, leaving the solution for a day, and titrating the liberated iodine against the standard thiosulphate solution. Magnesium chloride solutions were standardised against EDTA, and lithium and lanthanum chloride solutions against silver nitrate.

Procedure.—Most experiments (Table 1) were carried out with 200 ml. of a solution containing 0·0025M-potassium iodide, 0·000125M-potassium persulphate, 0·0005M-hydrochloric acid, 5×10^{-6}M-EDTA (as disodium salt), and an added electrolyte. The reaction vessel was in a thermostat at 25° ± 0·02° and was completely shielded from light.

Successive accurately known additions of 0·01 ml. of 0·01M-sodium thiosulphate solution

Table 1. *Second-order rate-constants,* 10^3k *(l. mole*$^{-1}$ *sec.*$^{-1}$*), for the reaction of* $S_2O_8^{2-}$ *with* I^- *at 25°.*

$[K_2S_2O_8] = 1·25 \times 10^{-4}$, $[KI] = 2·50 \times 10^{-3}$, $[HCl] = 5 \times 10^{-4}$, $[EDTA] = 5 \times 10^{-6}$ mole l.$^{-1}$, $10^3k = 1·26$ l. mole^{-1} sec.$^{-1}$.

Equiv. l.$^{-1}$	0·005	0·01	0·02	0·04	0·1
Added salt					
KCl(1)	1·52	1·77	2·13	2·70	4·12
$KClO_4$(2)	—	1·75	2·11	2·67	—
KNO_3(3)	1·56	1·86	2·21	2·79	4·24
K_2SO_4(4)	1·53	1·75	2·11	2·65	3·82
NaCl(5)	—	—	1·77	2·12	2·84
$NaClO_4$(6)	—	—	1·90	2·28	3·05
Na_2SO_4(7)	1·44	1·54	1·76	2·08	2·73
$Na_3P_3O_9$(8)	—	—	1·80	2·11	2·73
$Na_4P_4O_{12}$(9)	—	1·54	1·72	2·03	—
LiCl(10)	—	—	1·67	1·91	2·43
NMe_4Br(11)	—	—	—	1·89	2·22
NEt_4Br(12)	—	—	—	1·48	1·40
$MgCl_2$(13)	1·74	2·06	2·44	2·89	3·58
$LaCl_3$(14)	—	4·35	5·32	—	—
$Co(NH_3)_6Cl_3$(15)	13·85 *	25·2	—	38·7	—

* 0·0025 equiv. l.$^{-1}$.

were made from an " Agla " micrometer syringe. On each occasion, the time at which the thiosulphate had been completely consumed by the iodine produced was determined by a polarised electrode method. Two platinum wires, each 1" long, dipped into the solution and were connected in series with a 27v dry battery and a 20 megohm resistance as a constant-current source; a Tinsley 4500 LS galvanometer with a 1·8 megohm resistance in series was used as a voltmeter. The solution was stirred by an electric motor whose speed was maintained constant with a manually controlled resistance and a stroboscope. Both the thiosulphate and iodine depolarise the electrodes and the potential difference between the electrodes rises to a maximum when neither is present. It was found convenient to treat as the end-point a time when the galvanometer deflection had fallen a small but definite amount below the maximum.

[21] Indelli, *Ann. Chim.* (*Italy*), 1953, **43**, 845.
[22] *Idem, ibid.*, 1957, **47**, 586.

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Usually 15 to 20 points were determined on the reaction curve for each solution. Iodide ions are constantly regenerated by the reaction of the iodine produced with the added thiosulphate and the reaction under these conditions behaves as a first-order one. Fig. 1 shows a typical first-order plot for a reaction in 0·1M-sodium chloride, in which C_0 and C_t are the persulphate-ion concentrations at times 0 and t. Because of the sensitivity of the polarised-electrode method of end-point determination and the use of the microsyringe, we believe that we have been able to determine rate constants accurate to within 1—2% by a study of only about 4% of the reaction; the deviations of the individual points from the first-order plots correspond to 10^{-6} mole/l of I_2. The good first-order plots and the very small change in the composition of the solutions during a measurement support the necessary assumption that throughout a measurement the concentration of thiosulphate (or iodine) at each potential maximum is the same even if not exactly zero.

All solutions were 0·0005M in hydrochloric acid because preliminary experiments showed that the acid eliminated an induction period. The solutions were also 5×10^{-6}M in EDTA because otherwise the reaction rates were higher and less reproducible; presumably EDTA removes traces of heavy-metal ions with a strong catalytic effect. A tenfold increase in the concentration of EDTA did not affect the rates. No complications could arise from the presence of I_3^- ions, for their concentration is always negligible compared with that of iodide ions. Ordinarily the thiosulphate was only present for a very short time, but the possibility that reaction between thiosulphate and persulphate ions was a source of error was eliminated by performing some experiments in which the concentrations of thiosulphate and persulphate were both increased tenfold and the thiosulphate was added immediately after the appearance of iodine; the observed rates did not differ by more than 4% from those ordinarily obtained.

TABLE 2. *Second-order rate-constants for the reaction of* $S_2O_8^{2-}$ *with* I^- *at* 25°

Except in last entry $[K_2S_2O_8] = 1{\cdot}25 \times 10^{-3}$, $[KI] = 2{\cdot}50 \times 10^{-3}$, $[HCl] = 5 \times 10^{-4}$ mole l.$^{-1}$, $[EDTA] = 5 \times 10^{-6}$ mole l.$^{-1}$.

Added salt	—	NaCl	NaCl	$NaClO_4$	$NaClO_4$	$Na_3P_3O_9$	$Na_3P_3O_9$	$Na_4P_4O_{12}$	NaI *
Concn. (equiv. l.$^{-1}$) ...	—	0·02	0·10	0·02	0·10	0·02	0·10	0·02	0·0025
10^3k (l. mole^{-1} sec.$^{-1}$)...	1·30	1·78	2·85	1·80	2·86	1·81	2·83	1·72	1·19

* KI omitted, $[K_2S_2O_6] = 1{\cdot}25 \times 10^{-4}$ mole l.$^{-1}$.

If there were any appreciable reaction between persulphate and tetrathionate ions one would not expect linear first-order plots.

The results of a few experiments with a concentration of potassium persulphate ten times greater than usual, or with sodium iodide replacing potassium iodide, are given in Table 2.

DISCUSSION

The logarithms of the second-order rate-constants in Table 1 have been plotted in Fig. 2 against the square-root of the ionic strength. The numbering of the added salts in Table 1 corresponds to that in Figs. 2 and 3. For clarity the experimental points are not shown; none deviates by more than 2% from its curve. Fig. 2 also shows the Debye–Hückel limiting-law slopes for reactions of various charge types. The primary kinetic salt effects observed are positive but very specific, and seldom even approximate to the behaviour predicted by the limiting law for a reaction between singly- and doubly-negatively charged ions. For most salts, attempts to describe the results up to an ionic strength of 0·1 by the equation previously found successful [7] for the reaction between potassium bromoacetate and potassium thiosulphate also fail. It is also clear that association of the activated complex with cations cannot alone adequately explain the results both because many of the salt effects are much less than the Debye–Hückel equation predicts, and also because of the pronounced specific effects of anions. Although the results for potassium chloride and potassium sulphate can be described to within 5% by assuming that there are two reaction paths, in the second of which the activated complex contains a potassium ion as well as the persulphate and iodide ions, yet attempts to extend this treatment to other salts by postulating the association of reactant ions fail.

The magnitude of the specific effects of the cations is evident both from the very large influence of the triply charged cations and from the observation that even when the ionic strength is as low as 0·0034 mole l.$^{-1}$, replacement of the 0·0025M-potassium iodide by sodium iodide reduces the rate by 5%. If the rate constant is plotted against the equivalent concentration of cations (Fig. 3), the curves for the various sodium and potassium salts

FIG. 1.

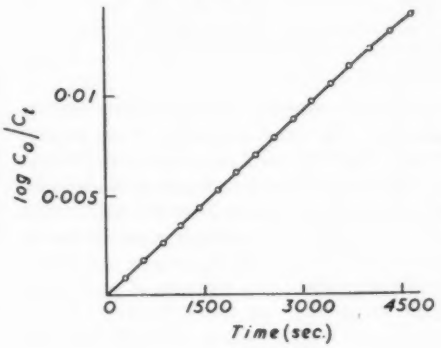


FIG. 2.

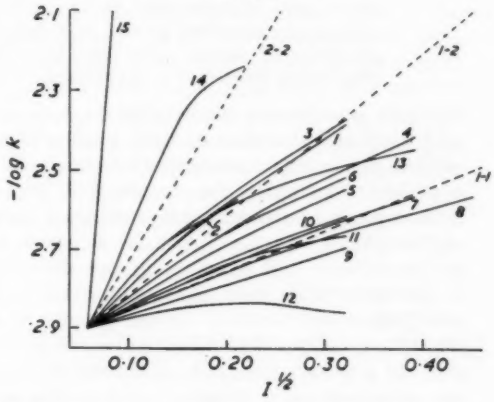
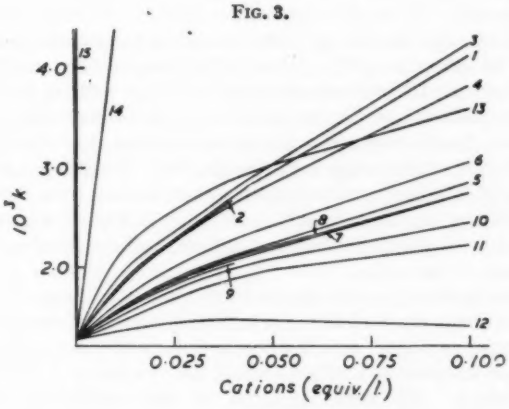


FIG. 3.



fall in sheafs corresponding to the cation and to this extent there is a better correlation of the rate constants with the concentration and character of ions of charge opposite to that of the reactants than with the ionic strength, but we note also the differences between the curves for uni-univalent salts of the same cation. We conclude that over the ionic strength range studied, the specific effects exerted by both cations and anions on the large triply charged activated complex with unknown charge distribution outweigh completely the long-range interactions described by the Debye–Hückel equations; nor does the additional assumption of ion association seem capable of providing a satisfactory interpretation of the results.

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THE UNIVERSITY, READING.

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24. *A General Stereoselective Synthesis of Olefins.*

By J. W. Cornforth, (Mrs.) R. H. Cornforth, and K. K. Mathew.

The addition of Grignard reagents or lithium alkyls to aliphatic α-chlorocarbonyl compounds is shown to be a stereoselective process. The chlorohydrins produced are converted into olefins by three stereospecific steps, the intermediates being epoxides and iodohydrins. A new procedure for making iodohydrins from epoxides, and a new reagent for reduction of iodohydrins to olefins, are described, as well as a direct but non-stereospecific reduction of epoxides to olefins. The geometry of the two 3-methylpent-2-enes is established by unequivocal synthesis of each isomer.

An olefin is commonly made either from an acetylene by addition of hydrogen or from a more saturated structure by some kind of elimination. By using acetylides most monoalkylethylenes and 1 : 2-dialkylethylenes can be made, the latter with *cis*- or *trans*-geometry as desired; but unless the chemistry of lithium alkenyls can be developed more widely than at present seems probable, acetylenes show little promise as sources of tri- and tetraalkylethylenes. On the other hand, ethylenes with any degree of substitution can be made by elimination; but when the groups eliminated are H and X, the hydrogen can often be abstracted from more than one position, so that the product is a mixture of positional and geometrical isomers. When groups X and Y (neither of them hydrogen) are eliminated, the position of the double bond is determined if it is formed in conditions too mild for a prototropic shift; the chemical problem is then to prepare CabX·CcdY, and the stereochemical problem is to obtain this in the desired configuration and to make the elimination stereospecific. Formation of olefins from 1 : 2-dibromides and zinc is one stereospecific (*trans*) elimination, but an olefin is usually the starting point for preparation of the dibromide. In Boord's synthesis [1] a 1 : 2-dibromo-ether reacts with a Grignard reagent to give a substituted 2-bromo-ether from which an olefin is prepared by the action of zinc. This method, which has affinities with the one to be described, is useful for making a carbon chain with a double bond at a particular position, but it is less satisfactory for trisubstituted olefins and neither stage is stereoselective. A related synthesis,[2] the scission by sodium of 2-alkyl-3-chlorotetrahydropyrans, is a useful source of *trans*-4-en-1-ols, but is of limited scope. Wittig and Schöllkopf's admirable method,[3] which has almost every attribute of a truly general synthesis of olefins, suffers from the disadvantage that mixtures of geometrical isomers are formed.

The hydrocarbon squalene, an intermediate in the biosynthesis of cholesterol, has six trisubstituted double bonds of which four can exhibit geometrical isomerism. The problem of synthesising all-*trans*-squalene, and if necessary some of its nine geometrical isomers, impressed on us that no general method existed for obtaining a trisubstituted olefin of predetermined geometry. We were attracted by the possibility of a stereoselective synthesis of a halogenohydrin, followed by stereospecific elimination of the elements of hypohalous acid.

Reaction of α-Chloro-carbonyl Compounds with Organometallic Reagents.—Grignard reagents add normally to the carbonyl group of chloroacetone,[4] though rearrangement may subsequently occur if the reaction mixture is heated.[5] Chloroacetaldehyde likewise can react normally with ethylmagnesium bromide.[6] Our experience confirms that many α-chloro-aldehydes and α-chloro-ketones react smoothly with Grignard reagents to give

[1] Boord *et al.*, *J. Amer. Chem. Soc.*, 1930, **52**, 651, 3396; 1931, **53**, 1505; 1932, **54**, 751; 1933, **55**, 3293, 4930.

[2] Crombie and Harper, *J.*, 1950, 1707; Crombie, Gold, Harper, and Stokes, *J.*, 1956, 136; cf. Riobé, *Compt. rend.*, 1947, **225**, 334; Brandon, Derfer, and Boord, *J. Amer. Chem. Soc.*, 1950, **72**, 2120.

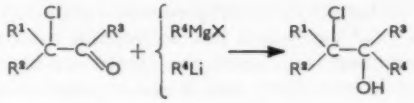
[3] Wittig and Schöllkopf, *Ber.*, 1954, **87**, 1318.

[4] Tiffeneau, *Compt. rend.*, 1902, **134**, 774.

[5] Henry, *ibid.*, 1907, **145**, 24.

[6] Helferich and Speidel, *Ber.*, 1921, **54**, 2636.

chlorohydrins, and we find also that lithium alkyls react in the same sense. The general reaction is:

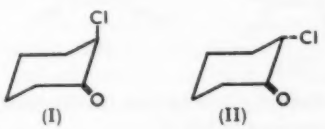


We habitually mix the reagents at −70° and add acetic acid soon afterwards to decompose the complex. This technique, adopted to minimise rearrangement of the complex, is so rapid and convenient that there has been no incentive to compare it with operation at room temperature; with the one (Grignard) reaction where such a comparison was made, the yield at the higher temperature was a little lower. Comparisons of lithium alkyls with Grignard reagents were made more extensively. In general, the Grignard reagent gave the superior yield of chlorohydrin from substances containing the group $-CO\cdot CH_2Cl$, probably because the lithium alkyl induced self-condensation of the ketone. The lithium alkyl had the advantage with more hindered carbonyl compounds; these are less prone to enolisation but are liable to reduction by the Grignard reagent. Comparative yields are assembled in the Table.

Chloro-carbonyl compound	Yield (%) with Bu^nLi	Yield (%) with Bu^nMgBr	Chloro-carbonyl compound	Yield (%) with Bu^nLi	Yield (%) with Bu^nMgBr
$CH_3\cdot CH_2\cdot CHCl\cdot CHO$	65	68	$CH_3\cdot CO\cdot CHCl\cdot CH_3$	79	65
$CH_3\cdot CO\cdot CH_2Cl$	30 *	67	$(CH_3)_2CCl\cdot CHO$	63	25
$CH_3\cdot CH_2\cdot CO\cdot CH_2Cl$	25	75	$(CH_3)_2CCl\cdot CO\cdot CH_3$	68	10

* Light petroleum, not ether, used as solvent.

The stereochemistry of nucleophilic addition to the carbonyl group of aliphatic α-chloro-carbonyl compounds had never been investigated. We were first attracted to this as a possibly stereoselective process by Corey's statements [7] that 2-chloro*cyclo*hexanone in the liquid state exists entirely in the form (I) with axial chlorine, and that this is in accord with theoretical calculations, the compression of axial substituents in (I) being outweighed by the electrostatic repulsion of C=O and C–Cl dipoles in the " equatorial " conformation (II). Such a repulsion might check free rotation about the C–C bond in aliphatic $-CO-CCl<$ and irreversible additions to the C=O group should then be stereoselective. However, it has been shown [8] that the predilection for axial halogen in the related 2-bromo*cyclo*hexanone is not absolute; and work by Bellamy *et al.*[9] with the acyclic α-chloro-carbonyl group (chloroacetone, ω-chloroacetophenone, etc.) indicates that in the liquid state two rotational isomers are present and that in the more stable of these the C=O and C–Cl groups are eclipsed (III).



(I) (II) (III)

All these findings were based on measurements of C=O stretching frequencies: when the infrared spectrum of a steroid α-bromo-ketone of known configuration was compared with the spectrum of the parent ketone, the C=O stretching absorption was found at a higher frequency if the C=O and C–Br bonds were approximately in the same plane.[10]

[7] Corey, *J. Amer. Chem. Soc.*, 1953, **75**, 2301; Corey and Burke, *ibid.*, 1955, **77**, 5418.
[8] Allinger and Allinger, *Tetrahedron*, 1958, **2**, 64.
[9] Bellamy, Thomas, and Williams, *J.*, 1956, 3704; Bellamy and Williams, *J.*, 1957, 4294.
[10] (*a*) Jones, Ramsay, Herling, and Dobriner, *J. Amer. Chem. Soc.*, 1952, **74**, 2828; (*b*) Jones, *ibid.*, 1953, **75**, 4839; (*c*) Dickson and Page, *J.*, 1955, 447.

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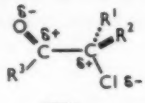
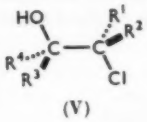
The effect was explained as an interaction of dipoles, the polarity of the C–Br bond reducing that of the C=O bond [10a] (Bellamy [11] mistakenly reports the opposite conclusion).

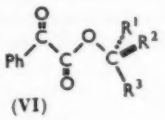
This intramolecular field effect in the eclipsed conformation (III) would thus resist the separation of charge, $>C^{\delta+}=O^{\delta-}$, on which the electrophilic reactivity of a carbonyl group depends. In the conformation (IV), where the dipoles are antiparallel, the polarisation of the carbonyl group would be easiest; and, if ease of polarisation has a marked effect on the energy required to form the transition state with a nucleophilic agent, the chloroketone might react largely in conformation (IV), even though this form made little contribution to the rotational equilibrium in solution. Steric hindrance would operate to favour the attack of the nucleophilic agent on that side of the carbonyl group which is shielded by the smaller of the groups R^1, R^2. The situation is similar to that envisaged in Cram's rule.[12] Thus, when a nucleophilic agent R^4X reacts irreversibly with an α-chloroketone (or α-chloro-aldehyde) $R^1R^2ClC{\cdot}COR^3$, the resulting chlorohydrin would have a preponderance of molecules (V) wherein R^4 is *anti* to the larger (here R^2) of the two groups R^1, R^2 when the chlorine and hydroxyl groups are *anti* to each other.



(IV)



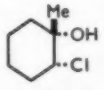
(V)



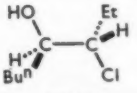
(VI)

It seems possible that Prelog's method [13] for determining the absolute configuration of alcohols may in part owe its success to a similar effect. In considering the steric effects of the groups R^1, R^2, R^3 on the addition of methylmagnesium iodide to the phenylglyoxylate (VI) of an asymmetric alcohol, Prelog assumed that the overwhelming majority of molecules in the ester had the *transoid* conformation (VI). However, the marked exaltation of carbonyl stretching frequencies found in methyl pyruvate [14] suggests that a *transoid* relation of carbonyl groups is not always preferred in α-oxo-esters. On the other hand, the polarisation effects should make the form (VI) the most reactive of all rotational isomers.

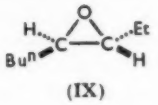
Addition of methylmagnesium halide to 2-chloro- and 2-bromo-*cyclo*hexanones has been shown [15,16] to yield predominantly *cis*-halogenohydrins (VII), and reduction of 2-chloro-*cyclo*hexanone by *tert.*-butylmagnesium chloride gives largely *cis*-2-chloro*cyclo*hexanol.[17] Since 2-chloro*cyclo*hexanone normally prefers the conformation with axial chlorine this would be the expected result even if polarisation effects are disregarded, but it is also explained by the arguments developed above which indicate that the conformation with



(VII)



(VIII)



(IX)

axial chlorine is the more reactive. 2-Methyl*cyclo*hexanone, in contrast, gives a mixture of two isomers by addition of methylmagnesium halide.[18]

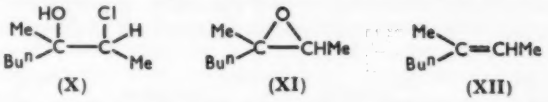
To discover whether the addition of organometallic reagents to aliphatic α-chlorocarbonyl compounds was stereoselective in the predicted direction, it was necessary to

[11] Bellamy, "The Infrared Spectra of Complex Molecules," Methuen, London, 1954, p. 121.
[12] Cram and Elhafez, *J. Amer. Chem. Soc.*, 1952, **74**, 5828.
[13] Prelog, *Helv. Chim. Acta*, 1953, **36**, 308.
[14] Randall, Fowler, Fuson, and Dangl, "Infra-red Determination of Organic Structures," Van Nostrand, New York, 1949.
[15] Tiffeneau and Tchoubar, *Compt. rend.*, 1934, **199**, 360.
[16] Bartlett and Rosenwald, *J. Amer. Chem. Soc.*, 1934, **56**, 1990.
[17] Bartlett, *ibid.*, 1935, **57**, 224.
[18] Chiordoglu, *Bull. Soc. chim. belges*, 1938, **47**, 241.

make by this method a chlorohydrin of ascertainable configuration. A suitable example was 3-chloro-octan-4-ol, which we prepared from 2-chlorobutanol and butylmagnesium bromide or butyl-lithium. The chlorohydrin was converted by aqueous alkali into 3 : 4-epoxyoctane. This type of reaction is well established as a nucleophilic displacement with inversion at the halogen-bearing carbon atom. Thus, if the chlorohydrin had the expected preponderance of the stereoisomeride (VIII), the epoxide would consist mainly of (IX), the product obtainable by (*cis*-)epoxidation of *trans*-oct-3-ene. From 3-octyne, samples of *trans*-oct-3-ene (by reduction with sodium in ammonia [19]) and *cis*-oct-3-ene (by hydrogenation over Lindlar catalyst) were obtained and each was oxidised by monoperphthalic acid. Mixtures of the two epoxides were made and the infrared spectra were compared with that of the epoxide from the chlorohydrin; this epoxide proved to be a mixture containing about 70% of *trans*-epoxide (IX), and the composition was almost the same whether a Grignard reagent or a lithium alkyl had been used to make the chlorohydrin, though the chlorohydrin from the Grignard reaction gave slightly more *trans*-epoxide. Stereoselectivity of this degree * was considered satisfactory in a reaction with an α-chloro-aldehyde. Access to the carbonyl group in an α-chloro-ketone is more restricted: higher selectivity could then be expected and was indeed observed.

Preparation of Olefins from Chlorohydrins.—We abandoned, after several trials, the attempt to eliminate from chlorohydrins the elements of hypochlorous acid. An obvious variant was the conversion of the chlorohydrin *via* the epoxide into a bromohydrin, for bromohydrins have long been known [20] to give olefins on treatment with zinc.† Since formation of the epoxide and of the bromohydrin would each proceed with inversion at one carbon atom, the stereochemistry of the bromohydrin, for the purpose of an elimination, would correspond to that of the chlorohydrin even if the positions of hydroxyl and halogen were partially or wholly interchanged.

Many orienting experiments were made with 2-chloro-3-methylheptan-3-ol (X), prepared from 3-chlorobutan-2-one and butylmagnesium bromide or butyl-lithium. 2 : 3-Epoxy-3-methylheptane (XI) was readily made by stirring the chlorohydrin with aqueous sodium hydroxide. A bromohydrin was prepared by slow addition of hydrobromic acid to a solution of this epoxide in acetone containing lithium bromide and a little Thymol Blue. When the bromohydrin was treated with zinc powder in acetic acid an



(X) (XI) (XII)

olefin was obtained, along with a higher-boiling ketonic fraction. The yield of olefin from epoxide was 25%. In a similar experiment using sodium iodide–hydriodic acid instead of lithium bromide–hydrobromic acid the yield was rather better (39%). Reduction of an iodohydrin to an olefin does not seem to have been reported previously.

When the epoxide (XI) was added to sodium iodide in acetic acid, an iodohydrin was formed rapidly, and subsequent addition of zinc powder gave an olefin, isolated in 56% yield. Two further refinements were then discovered: when the epoxide was added to a

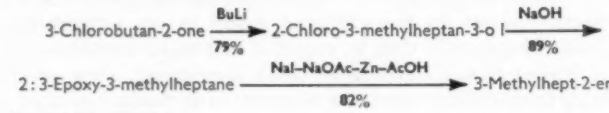
* The stereochemical purity of our *cis*-oct-3-ene was not proved; if it contained a small proportion of *trans*-oct-3-ene the stereoselectivity in the formation of 3-chloro-octan-4-ol could have been slightly higher than 7 : 3.

† Three apparent exceptions to this rule were reported by Barton, Lewis, and McGhie: [21] it was claimed that 2α- and 2β-bromolanost-8-en-3β-ol and 2α-bromolanostan-3β-ol were reduced to the *alcohols* in 80—85% yields by zinc. When the procedures described for debromination of 2α-bromolanost-8-en-3β-ol and 2β-bromolanost-8-en-3β-ol were repeated in this laboratory, the former was entirely unchanged and the latter gave as principal product lanost-8-en-3-one along with some lanost-8-en-3β-ol, lanost-8-en-3β-yl acetate, and a little lanosta-2 : 8-diene. Dr. McGhie (personal communication) kindly checked our findings and confirmed them; he suggested that the earlier results were obtained with an exceptional batch of zinc.

[19] Henne and Greenlee, *J. Amer. Chem. Soc.*, 1943, **65**, 2020.
[20] Mokiewsky, *J. Russ. Phys.-Chem. Soc.*, 1898, **30**, 900; *Chem. Zentr.*, 1899, I, 591.

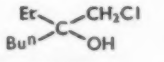
cooled stirred mixture of zinc powder, sodium iodide, and acetic acid the olefin was obtained directly in 67% yield (in formic acid, 53%; in propionic acid, 70%). Finally, when the mixture of acetic acid, sodium iodide, and zinc was buffered by sodium acetate a 76% yield of olefin was secured and raised to 82% by working on a larger scale. In this composite process, protonation of the epoxide is presumably followed by nucleophilic addition of iodide ion, and then reduction of the iodohydrin before solvolytic processes can destroy much of it. Iodide ion consumed in the second stage is regenerated in the third, so that a catalytic amount of sodium iodide should, and does, suffice to promote olefin formation; but 3 : 4-epoxyoctane gave a lower yield of oct-3-ene with 0·2 equivalent of sodium iodide than with 2 equivalents.

The olefin from reduction of the epoxide (XI) was identified as 3-methylhept-2-ene (XII) by oxidation with the periodate–permanganate reagent,[22] which gave hexan-2-one in good yield. This olefin had not previously been obtained free from positional isomers.[23] The synthesis may be summarised thus:

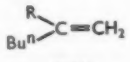


and the overall yield is 57·5%.

The scope of the synthesis was then explored. To obtain a 1 : 1-disubstituted olefin, 1-chlorobutan-2-one was treated with butylmagnesium bromide to give 3-chloromethylheptan-3-ol (XIII); the epoxide from this was reduced to 2-ethylhex-1-ene (XIV; R = Et). The olefin was identified by periodate–permanganate oxidation to heptan-3-one, and by its infrared spectrum which showed the expected bands at 887, 1647, 1775, and 3090 cm.$^{-1}$. 2-Methylhex-1-ene (XIV; R = Me) was prepared similarly from chloroacetone. 3 : 4-Epoxyoctane gave the 1 : 2-disubstituted ethylene, oct-3-ene. Another trisubstituted ethylene, 2-methylhept-2-ene (XV), was prepared from 2-chloro-2-methylpropanal. Finally the tetrasubstituted 2 : 3-dimethylhept-2-ene (XVI) was made from 3-chloro-3-methylbutan-2-one. Although no search was made for optimum conditions in these syntheses, the yields at all stages were satisfactory (lowest yield 63%). No monosubstituted ethylene (from chloroacetaldehyde) was made; presumably this could be done, but the process would never be so convenient as synthesis *via* an acetylene.



(XIII)



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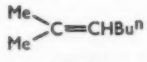
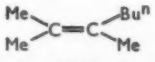


(XV)

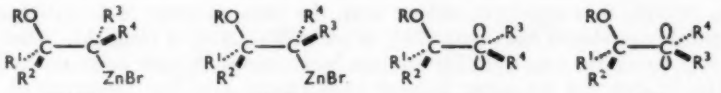


(XVI)

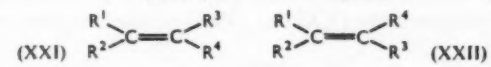
We had hoped that the reduction of iodohydrins to olefins might be a stereoselective *trans*-elimination; but reduction of the epoxide from either *trans*- or *cis*-oct-3-ene gave a mixture containing, as shown by infrared analysis, roughly equal parts of *trans*- and *cis*-olefins. House and Ro[24] recently reported similar results with some 2-bromo-ethers and 2-bromoalkyl acetates. They favoured, after discussion, the explanation that an organozinc compound (XVII) is formed first, and that this equilibrates (XVII $\rightleftharpoons$ XVIII) before (*trans*-)elimination of ZnBr and OR. However, it is hard to see why, if the molecules have no symmetry, forms (XVII) and (XVIII) should be formed in equal amounts; and even harder to devise for the interchange (XVII $\rightleftharpoons$ XVIII) a mechanism not involving separation of the ZnBr group. Once separation has occurred, reattachment of ZnBr to the carbanion is unlikely to be faster than attack by a proton from the medium

[21] Barton, Lewis, and McGhie, *J.*, 1957, 2907.
[22] Lemieux and Rudloff, *Canad. J. Chem.*, 1955, **33**, 1701.
[23] Church, Whitmore, and McGrew, *J. Amer. Chem. Soc.*, 1934, **56**, 176; cf. Obolentsev and Usof, *J. Gen. Chem. U.S.S.R.*, 1947, **17**, 899.
[24] House and Ro, *J. Amer. Chem. Soc.*, 1958, **80**, 182.

(ethanol or acetic acid). We offer the suggestion that these results and our own are explicable if the first step, as suggested by James, Reed, and Shoppee,[25] is removal of halogen by zinc to give a carbanion. This must be very short-lived to escape reaction with protons from the solvent, and hence elimination of OR may occur before much of the initial energy is dissipated by collisions. The excited state, we suggest, approaches a planar configuration in which the barrier to rotation about the C–C bond offered by the groups R^3, R^4 is lowered and the two states (XIX) and (XX), most favourable for elimination of OR, can equally well be reached. The two geometrical isomers of the olefin, (XXI and XXII), would then be formed in equal amounts.



(XVII) (XVIII) (XIX) (XX)

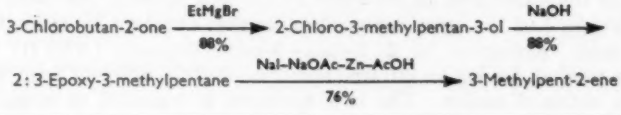


(XXI) (XXII)

Development of Stereospecific Elimination.—The one-stage reduction of epoxides is a useful method for making olefins when the position of the double bond is important and geometrical isomerism cannot occur or does not matter, but we sought a stereospecific elimination which would preserve the stereoselectivity found in the formation of chlorohydrins. Experiments with oct-3-ene were therefore continued. When the epoxide of *trans*-oct-3-ene was converted into an iodohydrin which was then treated with sodium hydroxide, the recovered epoxide was identical in configuration with the starting material; this proved that addition of hydrogen iodide proceeded, as expected, with inversion, and that elimination was the unselective stage in the formation of olefin.

Various modifications of this stage were then tried: use of smaller amounts of sodium iodide; use of lithium bromide instead of sodium iodide; reduction of the iodohydrin by magnesium, amalgamated aluminium, cadmium, a solution of zinc in mercury, or amalgamated zinc powder. All these procedures gave some oct-3-ene, but this was a 50 : 50 mixture of *cis*- and *trans*-isomers in every experiment except the last-mentioned, which gave a mixture containing 60% of *trans*-oct-3-ene from the *trans*-epoxide. Reduction of the iodohydrin from the *trans*-epoxide by chromous chloride in acetic–hydrochloric acid was more promising, the olefin (47% yield) containing 75—80% of *trans*-oct-3-ene. Finally, when the iodohydrin was reduced by stannous chloride in acetic–hydrochloric acid, a stereospecific elimination was achieved: each olefin, obtained in 70% yield from each epoxide, had an infrared spectrum identical with that of the olefin from which the epoxide was made. The mixture of epoxides obtained from 3-chloro-octan-4-ol, when reduced *via* the iodohydrin by stannous chloride, gave as expected a mixture of oct-3-enes containing about 70% of the *trans*-isomer.

We now required a geometrically isomeric pair of trisubstituted ethylenes. The two 3-methylpent-2-enes prepared by dehydration of 3-methylpentan-3-ol can be separated from each other, and from 2-ethylbut-1-ene, by fractional distillation.[26] We preferred our own method for making the mixture of 3-methylpent-2-enes:

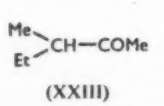


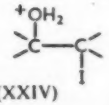
[25] James, Rees, and Shoppee, *J.*, 1955, 1370.
[26] Streiff, Zimmerman, Soule, Butt, Sedlak, Willingham, and Rossini, *J. Res. Nat. Bur. Stand.*, **1948**, **41**, 323; Streiff, Soule, Kennedy, James, Sedlak, Willingham, and Rossini, *ibid.*, 1950, **45**, 173.

XUM

This product was separated by distillation into the lower-boiling (olefin A) and higher-boiling (olefin B) isomers. These, like the oct-3-enes, were present in about equal amounts. Each was converted into a 2 : 3-epoxy-3-methylpentane (epoxides A and B). It was now possible to assess the stereoselectivity of the reaction between ethylmagnesium bromide and 3-chlorobutan-2-one by infrared analysis of the epoxide obtained from the product. This proved to be a mixture of 80—85% of epoxide B with 15—20% of epoxide A. Further, when 2-chloro-3-methylpentan-3-ol was prepared instead from 2-chloropentan-3-one and methylmagnesium bromide, the epoxide from this chlorohydrin had the infrared spectrum of a mixture of 80—85% of epoxide A and 15—20% of epoxide B.

Epoxides A and B were each converted into iodohydrins; when these were reduced by stannous chloride in acetic–hydrochloric acid, the same mixture of 3-methylpent-2-enes was regrettably produced from both (70% of olefin B + 30% of olefin A). Olefins A and B were each converted into a similar mixture by stannous chloride in acetic–hydrochloric acid. This change did not occur without hydrochloric acid, but treatment of the iodohydrin with stannous chloride in acetic acid gave only a little impure olefin: the main product was 3-methylpentan-2-one (XXIII). Various other modifications were then tried


(XXIII)

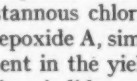

(XXIV)

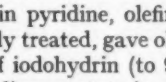
(XXV)

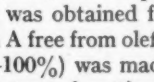
without success. Eventually it was recognised that the reduction of an iodohydrin by stannous chloride–hydrochloric acid was probably a two-step process: the first step would be a concerted elimination of the protonated hydroxyl group (in XXIV) to form a bridged iodonium ion (XXV), from which stannous chloride abstracted iodine in the reducing step. The concerted elimination would certainly require the four centres concerned (O–C–C–I) to be coplanar, with oxygen and iodine *anti* to each other; in the second step the incipient double bond in (XXV) would simply be developed as the iodine atom was withdrawn. The net result is a *trans*-elimination of HOI, as observed in the oct-3-ene series. If this analysis is correct, hydrochloric acid might be supplanted by some reagent which can dehydrate alcohols without isomerising olefins. Phosphoryl chloride in pyridine is such a reagent.

When the iodohydrin from epoxide B was treated with a mixture of phosphoryl chloride and anhydrous stannous chloride in pyridine, olefin B was obtained free from olefin A. Iodohydrin from epoxide A, similarly treated, gave olefin A free from olefin B.

An improvement in the yield of iodohydrin (to 97—100%) was made by treating the epoxide with sodium iodide and sodium acetate in a mixture of acetic and propionic acid at −20°. The reduction was improved in yield and convenience by dissolving stannous chloride in pyridine and adding first the iodohydrin and then a mixture of phosphoryl chloride and pyridine. When 3 : 4-epoxyoctane (XXVI), obtained from the chlorohydrin,


(XXVI)


(XXVII)

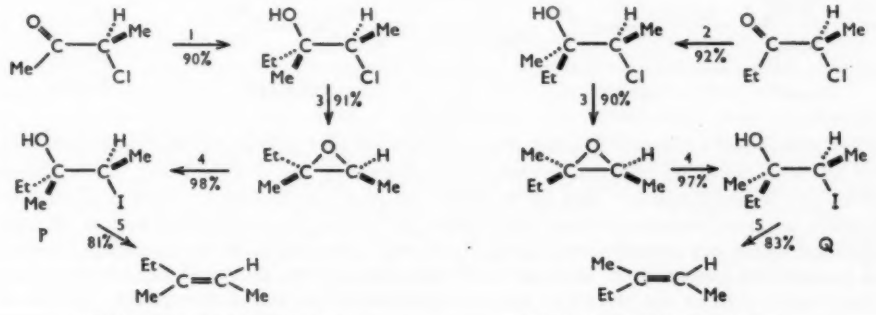

(XXVIII)

was reduced *via* the iodohydrin to oct-3-ene by the new method, the olefin (87% overall yield from epoxide) had the same composition as that obtained by reduction in acetic–hydrochloric acid. Reduction of 2 : 3-epoxy-3-methylheptane (XXVII) by the new method gave a product having an infrared spectrum slightly different from the product of zinc reduction obtained earlier. The new specimen is regarded as being very largely 3-methyl-*trans*-hept-2-ene (XXVIII).

Reduction of a chlorohydrin (2-chloro-3-methylheptan-3-ol) or a bromohydrin (2-bromo-3-methylpentan-3-ol) by the stannous chloride–phosphoryl chloride–pyridine

reagent gave no olefin; nor could phosphoryl chloride be replaced by thionyl chloride, acetyl chloride, or stannic chloride in the reduction of iodohydrins. A by-product of the reduction, especially if the reaction mixture is left for some time, is a small amount of yellow phosphorus; this is easily removed from the product by treatment with water and iodine.

Geometry of the Isomeric 3-*Methylpent-2-enes.*—The stereoselective synthesis of the 3-methylpent-2-enes proceeds, according to the views developed above, in accordance with the annexed scheme. Here the higher-boiling " olefin B " separated by fractionation of the two hexenes is 3-methyl-*trans*-pent-2-ene and the lower-boiling " olefin A " is



80—85% of 3-Methyl-*trans*-pent-2-ene, b. p. 70—71°

80—85% of 3-Methyl-*cis*-pent-2-ene, b. p. 68—69°

(Materials P and Q may contain isomers with interchanged positions of OH and I.)
Reagents: 1, EtMgBr. 2, MeMgBr. 3, NaOH. 4, NaI–NaOAc–AcOH–Et·CO_2H. 5, $SnCl_2$–$POCl_3$–C_5H_5N.
Percentages on the arrows are yields.

3-methyl-*cis*-pent-2-ene. This assignment would indicate the same stereochemical preference during addition to the carbonyl group of the chloro-ketone as was proved to exist in the synthesis of oct-3-ene. However, in many papers and works of reference, including the recent 3rd Supplement of Beilstein's " Handbuch," it is stated (occasionally with a query) that the lower-boiling isomer is 3-methyl-*trans*-pent-2-ene. The source of this tradition seems to lie in a statement by Goldwasser and Taylor [27] that van Risseghem [28] had assigned the *trans*-configuration to the lower-boiling isomer. No such assignment was, in truth, made in the paper cited; and in a more recent communication [29] van Risseghem seemed to favour the opposite conclusion (although the pictorial formula given for the *trans*-isomer is that of 3-methyl-*cis*-pent-2-ene, and conversely). This opinion was based on debrominations of 2 : 3-dibromo-3-methylpentanes obtained by differing methods; however, it was finally stated that no experimental fact permitted a certain assignment of configuration to either isomeride. We were in need of such an assignment, and therefore set out to prove the configurations by an unequivocal method. Fortunately we had recently made, for a different purpose, 5-hydroxy-3-methyl-*trans*-pent-3-enoic acid (XXIX) and 3-methylpent-3-eno-5-lactone [30] (XXX). These were reduced by lithium aluminium hydride to 3-methyl-*trans*-pent-2-ene-1 : 5-diol (XXXI; X = OH) and 3-methyl-*cis*-pent-2-ene-1 : 5-diol (XXXII; X = OH) respectively; the *cis*-diol was also prepared by reduction of the isomeric lactone (XXXIII). Each diol was converted into the dibromide (XXXI and XXXII; X = Br) by the Rydon method with triphenyl phosphite benzylobromide, and the dibromides were reduced by lithium aluminium hydride in dibutyl ether to the 3-methylpent-2-enes (XXXI and XXXII; X = H).

[27] Goldwasser and Taylor, *J. Amer. Chem. Soc.*, 1939, **61**, 1751.
[28] van Risseghem, *Bull. Soc. chim. belges*, 1938, **47**, 47.
[29] *Idem*, *Bull. Soc. chim. France*, 1952, 177.
[30] Cornforth, Cornforth, Youhotsky, Gore, and Popják, *Biochem. J.*, 1958, **69**, 146.

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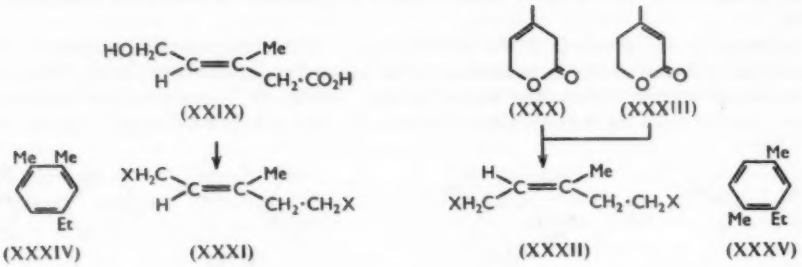
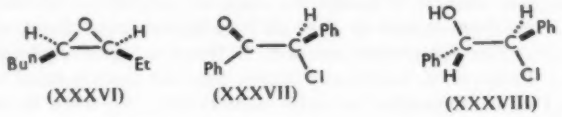
The methylpentene from the lactone (XXX) had an infrared spectrum almost identical with that of the lower-boiling olefin A; the infrared spectrum of the methylpentene from the hydroxy-acid (XXIX) was almost identical with that of the higher-boiling olefin B.



Harrison and Lythgoe [31] showed that replacement of a primary allylic hydroxyl group by bromine could be effected, without disturbance of the double bond, by triphenyl phosphite benzylobromide; and three reductions of allylic halides by lithium aluminium hydride without isomerisation are also known,[32,33] though an exception with a strongly hindered halide has recently been noted.[34] In any case a quantitative one-step *inversion* of geometrical isomerism in both *cis*- and *trans*-isomers, which would have had to take place here to confuse the two series, has no experimental or theoretical support. It follows that the lower-boiling olefin A is 3-methyl-*cis*-pent-2-ene (XXXII; X = H), and the higher-boiling olefin B is 3-methyl-*trans*-pent-2-ene (XXXI; X = H), in accord with prediction. Van Arkel's rule [35] incidentally leads to the same assignment: 1-ethyl-3 : 4-dimethylbenzene (XXXIV) is less volatile than 2-ethyl-1 : 4-dimethylbenzene [36] (XXXV). The infrared spectra of the two methylpentenes prepared by our method and separated by fractional distillation are in substantially complete agreement with the A.P.I.[37] spectra, provided that the A.P.I. assignments of configuration are reversed.

Reduction of an Aliphatic α-Chloro-ketone by Sodium Borohydride.—Because stereoselective addition to the carbonyl group of an α-chloro-ketone should be possible with other than organometallic reagents, we prepared 3-chloro-octan-4-one by oxidation of the alcohol and reduced it with sodium borohydride in aqueous ethanol. The product was converted by alkali into a 3 : 4-epoxyoctane which proved on infrared analysis to be a mixture of 80—85% of *cis*-epoxide (XXXVI) and 15—20% of *trans*. Reduction by the



stereospecific procedure duly gave a mixture of 80—85% of *cis*-oct-3-ene and 15—20% of *trans*-oct-3-ene; the borohydride reduction had therefore been stereoselective in the expected sense.

Reduction of the chloro-ketone (XXXVII) by lithium aluminium hydride in ether has been stated [38] to give exclusively the *erythro*-chlorohydrin (XXXVIII); but another

[31] Harrison and Lythgoe, *J.*, 1958, 843.
[32] Hatch and Perry, *J. Amer. Chem. Soc.*, 1949, **71**, 3262.
[33] Trevoy and Brown, *ibid.*, p. 1675.
[34] Corey, Chow, and Scherrer, *ibid.*, 1957, **79**, 5773.
[35] van Arkel, *Rec. Trav. chim.*, 1933, **52**, 1013.
[36] Birch, Dean, Fidler, and Lowry, *J. Amer. Chem. Soc.*, 1949, **71**, 1362.
[37] A.P.I. Research Project 44, "Catalog of Infrared Spectral Data," Nos. 720, 1061.
[38] Lutz, Wayland, and France, *J. Amer. Chem. Soc.*, 1950, **72**, 5511.

paper [39] published about the same time reported equal amounts of the *erythro*- and the *threo*-form. The *threo*-form would be expected to predominate by analogy with the reduction of 3-chloro-octan-4-one. Whether this discrepancy is caused by the presence of aromatic rings or by the use of different reducing agents is uncertain. However, it may be significant that 2-chloro*cyclo*hexanone, which with methylmagnesium bromide [15,16] gives almost entirely the chlorohydrin (VII) and with *tert.*-butylmagnesium chloride is reduced to *cis*-2-chloro*cyclo*hexanol,[17] gives a mixture of *cis*- and *trans*-2-chloro*cyclo*hexanols on reduction by lithium aluminium hydride.[39]

The stereochemistry of addition of some other reagents to α-chloro-ketones is at present being studied.

Experimental

Details of some exploratory experiments mentioned in the general section are not given here, but may be found in the Ph.D. thesis of K. K. M. (University of London, 1958).

General Procedure for Reaction of α-Halogenocarbonyl Compounds with Organometallic Reagents.—A 1·5—2M-ethereal solution of lithium alkyl or the Grignard reagent was prepared under nitrogen, cooled to −70°, and stirred during addition (10 min.) of the α-halogenocarbonyl compound dissolved in a little ether. After 10—15 min. a slight excess of acetic acid in ether was added; the mixture was brought to room temperature and diluted with water. The aqueous layer was extracted once with ether and the combined ethereal solutions were washed with water, aqueous sodium hydrogen carbonate, and water. From the dried ($MgSO_4$) solution the chlorohydrin was isolated by distillation at low pressure. The chlorohydrins were colourless liquids which usually darkened after a time.

3-*Chloro-octan*-4-*ol.*—(*a*) *n*-Butyl-lithium, prepared from lithium (1·8 g.), butyl bromide (17·7 g.), and ether (100 ml.), reacted with 2-chlorobutanal [40] (10 g.) to give 3-*chloro-octan*-4-*ol* (10 g., 64·5%), b. p. 94—96°/20 mm. (Found: C, 58·1; H, 10·3; Cl, 21·5. $C_8H_{17}OCl$ requires C, 58·3; H, 10·4; Cl, 21·5%).

(*b*) *n*-Butylmagnesium bromide, from magnesium (10 g.) and butyl bromide (54·8 g.) in ether (200 ml.), with 2-chlorobutanal (35·5 g.) gave the chlorohydrin (37 g., 67·5%), b. p. 96—99°/25 mm.

2-*Chloro*-3-*methylheptan*-3-*ol.*—(*a*) 3-Chlorobutan-2-one (21·3 g.) with *n*-butyl-lithium (from 3·6 g. of lithium and 34·2 g. of *n*-butyl bromide) gave 2-*chloro*-3-*methylheptan*-3-*ol* (X) (26 g., 79%), b. p. 81—82°/15 mm. (Found: C, 58·5; H, 10·6; Cl, 21·0. $C_8H_{17}OCl$ requires C, 58·3; H, 10·4; Cl, 21·5%).

(*b*) *n*-Butylmagnesium bromide, from magnesium (3·0 g.) and butyl bromide (17·1 g.), with 3-chlorobutan-2-one (10·65 g.) gave the chlorohydrin (10·6 g., 65%), b. p. 81—86°/20 mm., and an appreciable fraction, probably containing 3-chlorobutan-2-ol, b. p. 40—70°/20 mm.

3-*Chloromethylheptan*-3-*ol.*—(*a*) *n*-Butylmagnesium bromide, from magnesium (2·45 g.) and butyl bromide (13·7 g.), with 1-chlorobutan-2-one (8·2 g.) gave 3-*chloromethylheptan*-3-*ol* (XIII) (9·7 g., 75%), b. p. 81—88°/25 mm. Redistilled, it boiled at 85—86°/25 mm. (Found: C, 58·3; H, 10·3; Cl, 21·2. $C_8H_{17}OCl$ requires C, 58·3; H, 10·4; Cl, 21·5%).

(*b*) 1-Chlorobutan-2-one (21·3 g.) reacted with *n*-butyl-lithium to give after three distillations, a product (8 g.; b. p. 84—85°/20 mm.) presumably containing the chlorohydrin but impure (Found: C, 59·8; H, 10·3%).

1-*Chloro*-2-*methylhexan*-2-*ol.*—(*a*) *n*-Butylmagnesium bromide, from magnesium (3·0 g.) and butyl bromide (17·1 g.), with chloroacetone (9·3 g.) gave 1-*chloro*-2-*methylhexan*-2-*ol* (10·0 g., 67%), b. p. 74—78°/20 mm. (Found: C, 55·9; H, 9·9. $C_7H_{15}OCl$ requires C, 55·8; H, 10·0%).

(*b*) The reaction between chloroacetone (7 g.) and *n*-butyl-lithium (from 1·5 g. of lithium and 13·7 g. of butyl bromide) was carried out in light petroleum (b. p. 60—80°) instead of ether. The product (3·5 g.) had b. p. 76—82°/20 mm.

2-*Chloro*-2-*methylheptan*-3-*ol.*—(*a*) *n*-Butyl-lithium (from 1·2 g. of lithium and 12 g. of butyl bromide) with 2-chloro-2-methylpropanal (6·5 g.) gave 2-*chloro*-2-*methylheptan*-2-*ol* (6·3 g., 63%), b. p. 81—86°/20 mm. Redistilled, it had b. p. 82—83°/20 mm. (Found: C, 58·0; H, 10·6; Cl, 21·5. $C_8H_{17}OCl$ requires C, 58·3; H, 10·4; Cl, 21·5%).

[39] Felkin, *Compt. rend.*, 1950, **231**, 1316.
[40] Stevens, Farkas, and Gillis, *J. Amer. Chem. Soc.*, 1954, **76**, 2696.

(*b*) The chloro-aldehyde (9·5 g.) with *n*-butylmagnesium bromide (from 3·0 g. of magnesium and 17·1 g. of butyl bromide) gave the chlorohydrin (3·6 g., 24%), b. p. 81—85°/20 mm., and a lower fraction (4·0 g.; b. p. 40—70°/20 mm.).

2-Chloro-2 : 3-dimethylheptan-3-ol.—(*a*) *n*-Butyl-lithium (from 1·5 g. of lithium and 13·7 g. of butyl bromide), treated as usual with 3-chloro-3-methylbutan-2-one (10 g.), gave *2-chloro-2 : 3-dimethylheptan-3-ol* (10 g., 68%), b. p. 89—94°/25 mm. (91—93°/25 mm. after redistillation) (Found: C, 60·8; H, 11·1. $C_9H_{19}OCl$ requires C, 60·6; H, 10·7%).

(*b*) From the chloro-ketone (8 g.) and *n*-butylmagnesium bromide (from 2·0 g. of magnesium and 11·5 g. of butyl bromide) the major product had b. p. 40—45°/25 mm. and the yield of the chlorohydrin was 8% (1 g.; b. p. 90—98°/25 mm.).

2-Chloro-3-methylpentan-3-ol.—(a) "*Chlorohydrin* α." Methylmagnesium bromide, prepared from magnesium (16·5 g.), methyl bromide (45 ml.), and ether (250 ml.), was treated as usual with 2-chloropentan-3-one (60·25 g.). The product, *2-chloro-3-methylpentan-3-ol* α (62·7 g., 92%), was collected at 52—57°/18 mm. (Found: C, 52·5; H, 9·5; Cl, 26·4. $C_6H_{13}OCl$ requires C, 52·7; H, 9·6; Cl, 26·0%).

(b) "*Chlorohydrin* β." Ethylmagnesium bromide, from magnesium (24·3 g.), ethyl bromide (120 g.), and ether (400 ml.), reacted with 3-chlorobutan-2-one (79·9 g.; thrice fractionated to free it from 1-chlorobutan-2-one) to give 2-chloro-3-methylpentan-3-ol (91·8 g., 90%), b. p. 52—56°/16 mm. (Found: C, 52·5; H, 9·6; Cl, 25·9%). Fourneau and Tiffeneau [41] reported b. p. 160—165°.

Preparation of Epoxides.—The chlorohydrin was stirred with a slight excess of N-sodium hydroxide for 1—2 hr. and the product was extracted by ether and distilled.

From 3-chloro-octan-4-ol (7 g.) and N-sodium hydroxide (60 ml.; 1½ hr.) *3 : 4-epoxyoctane* (4·5 g.) was obtained, having b. p. 47·5—49°/20 mm. (Found: C, 74·9; H, 12·4. $C_8H_{16}O$ requires C, 74·9; H, 12·6%).

2-Chloro-3-methylheptan-3-ol (24·6 g.) and N-sodium hydroxide (190 ml.; 2 hr.) gave *2 : 3-epoxy-3-methylheptane* (17 g.; 88%), b. p. 42—44°/20 mm. (Found: C, 75·1; H, 12·4. $C_8H_{16}O$ requires C, 74·9; H, 12·6%).

1-Chloro-2-ethylhexan-2-ol (7·0 g.) and N-sodium hydroxide (60 ml.; 1½ hr.) gave *1 : 2-epoxy-2-ethylhexane* (1-n-*butyl*-1-*ethyloxiran*) (4·5 g.), b. p. 46°/20 mm., 150°/760 mm. (Found: C, 74·9; H, 12·4. $C_8H_{16}O$ requires C, 74·9; H, 12·6%).

1-Chloro-2-methylhexan-2-ol (7·6 g.) and N-sodium hydroxide (60 ml.; 1 hr.) gave *1 : 2-epoxy-2-methylhexane* (4·0 g.), b. p. 73°/110 mm. (Found: C, 73·2; H, 12·2. $C_7H_{14}O$ requires C, 73·6; H, 12·4%).

2-Chloro-2-methylheptan-3-ol (6·3 g.) and N-sodium hydroxide (50 ml.; 1½ hr.) gave *2 : 3-epoxy-2-methylheptane* (3·9 g.), b. p. 45—46°/25 mm. (Found: C, 74·6; H, 13·1. $C_8H_{16}O$ requires C, 74·9; H, 12·6%).

2-Chloro-2 : 3-dimethylheptan-3-ol (9 g.) and N-sodium hydroxide (70 ml.; 2 hr.) gave *2 : 3-epoxy-2 : 3-dimethylheptane* (5·9 g.), b. p. 57—58°/25 mm. (Found: C, 76·1; H, 12·8. $C_9H_{18}O$ requires C, 76·0; H, 12·8%).

2 : 3-Epoxy-3-methylpentane.—(a) "*Epoxide* α." 2-Chloro-3-methylpentan-3-ol ("chlorohydrin α;" 62·7 g.) was stirred vigorously with water (25 ml.) whilst 2·5N-sodium hydroxide (225 ml.) was added during ½ hr. After another 1½ hr. 2 : 3-epoxy-3-methylpentane α (41·4 g., 90%) was isolated by extraction with ether and distillation of the dried ($CaCl_2$) extract through a column; it had b. p. 98—103°/748 mm. A redistilled sample had b. p. 100—101° (Found: C, 71·7; H, 12·2. Calc. for $C_6H_{12}O$: C, 72·0; H, 12·1%).

(b) "*Epoxide* β." Prepared as above from "chlorohydrin β" (91·8 g.), 2 : 3-epoxy-3-methylpentane β (61·2 g., 91%) had b. p. 99—101°/750 mm., and 100—101° on redistillation (Found: C, 71·7; H, 12·3%).

cis-3 : 4-Epoxyoctane.—To 0·82M-ethereal monoperphthalic acid (75 ml.), *cis*-oct-3-ene (5·6 g.) was added at 5° and the mixture was kept at 0° overnight. Phthalic acid was removed by filtration and extraction with sodium hydroxide, and from the dried ($MgSO_4$) solution *cis-3 : 4-epoxyoctane* (4·0 g.), b. p. 47—49°/20 mm., was recovered (Found: C, 74·7; H, 12·6. $C_8H_{16}O$ requires C, 74·9; H, 12·6%).

trans-3 : 4-Epoxyoctane.—From *trans*-oct-3-ene (11·2 g.) and 1·15M-monoperphthalic acid in ether (100 ml.), *trans-3 : 4-epoxyoctane* (9·6 g.), b. p. 47—49°/20 mm., was obtained (Found: C, 74·9; H, 12·5%).

[41] Fourneau and Tiffeneau, *Compt. rend.*, 1907, **145**, 439.

trans-2 : 3-*Epoxy*-3-*methylpentane*.—3-Methyl-*trans*-pent-2-ene (5 g.) with ethereal 0·95M-monoperphthalic acid (80 ml.) gave the epoxide (4·2 g.), b. p. 97—99°. van Risseghem [39] gave b. p. 101·25—101·4° for a product which should be the *trans*-isomer from the method of preparation.

cis-2 : 3-*Epoxy*-3-*methylpentane* (4·35 g.) was prepared similarly from 3-methyl-*cis*-pent-2-ene (5 g.) and had b. p. 98—99° (Found: C, 71·6; H, 12·1. $C_6H_{12}O$ requires C, 72·0; H, 12·1%).

One-stage Preparation of Olefins from Epoxides.—This procedure was designed to permit isolation of the volatile olefins without use of solvents for extraction, and is illustrated by the preparation of 3-methylhept-2-ene. Sodium iodide (21 g.) and sodium acetate (7 g.; anhydrous) were dissolved in acetic acid (42 ml.) and water (3 ml.). To the ice-cooled stirred mixture zinc powder (21 g.) was added, and 2 : 3-epoxy-3-methylheptane (10·5 g.) was added dropwise during 10 min. After ¾—1 hr. the zinc residues were removed and washed with acetic acid. The filtrate after dilution with water was distilled until no more oil came over. The cooled distillate was neutralised by solid potassium hydroxide, and the aqueous layer was removed. The organic layer was dried (KOH) and distilled, to give 3-*methylhept*-2-*ene* (7·53 g., 82%), b. p. 121—123°. Redistilled through a column it had b. p. 121·5°, n_D^{25} 1·4170 (Found: C, 85·2; H, 14·0. C_8H_{16} requires C, 85·6; H, 14·4%). This product is presumably a mixture of about equal parts of *cis*- and *trans*-isomers.

Oxidation of 3-*Methylhept*-2-*ene*.—To the olefin (32 mg.), mixed with water (50 ml.) and potassium carbonate (25 mg.), was added the periodate–permanganate reagent [22] (25 ml.). The mixture was shaken until the oil disappeared (10 min.) and set aside for 18 hr. M-Sodium arsenite (15 ml.) was added and the volatile products were distilled into an ice-cooled receiver. The distillate (20 ml.) was treated with excess of 2 : 4-dinitrophenylhydrazine sulphate; after 1 hr. the solid product was collected (52 mg.; m. p. 98—102°). Recrystallised from dilute ethanol, it had m. p. 104—105° undepressed on admixture with hexan-2-one 2 : 4-dinitrophenylhydrazone, m. p. 106°. In another experiment the distillate was treated with hydroxylamine hydrochloride and titrated potentiometrically to pH 4·1. The acid liberated by oxime formation corresponded to an 84% yield of ketone from the olefin.

2-*Ethylhex*-1-*ene*.—Prepared as above from 1 : 2-epoxy-2-ethylhexane (2·5 g.), 2-ethylhex-1-ene (1·82 g., 80%) had b. p. 117—118° (b. p. 117·5°, n_D^{22} 1·4154, on redistillation) (Found: C, 85·4; H, 14·5. Calc. for C_8H_{16}: C, 85·6; H, 14·4%).

Oxidation of 2-*Ethylhex*-1-*ene*.—The olefin (32 mg.) was oxidised as described for 3-methylhept-2-ene. Formaldehyde was detected in the distillate by chromotropic acid, and was oxidised by treatment with 30% hydrogen peroxide (0·1 ml.) and 0·05N-sodium hydroxide (4 ml.). Back-titration showed consumption of 1·25 ml. of 0·05N-alkali. Excess of 2 : 4-dinitrophenylhydrazine sulphate was added and the solid product (35 mg.) was collected and recrystallised from aqueous ethanol; it had m. p. 78—82° and a mixture with heptan-3-one 2 : 4-dinitrophenylhydrazone (m. p. 79—81°) had m. p. 78—80°.

2-*Methylhex*-1-*ene*.—1 : 2-Epoxy-2-methylhexane (3 g.) was reduced as usual to give 2-methylhex-1-ene (1·8 g.), b. p. 92—93° after redistillation (Found: C, 85·1; H, 14·8. Calc. for C_7H_{14}: C, 85·6; H, 14·4%).

2-*Methylhept*-2-*ene*.—2 : 3-Epoxy-2-methylheptane (1·5 g.) similarly gave 2-methylhept-2-ene (0·9 g.; b. p. 122—125°), b. p. 122—123°, n_D^{22} 1·4172, on redistillation (Found: C, 84·8; H, 14·6. Calc. for C_8H_{16}: C, 85·6; H, 14·4%).

2 : 3-*Dimethylhept*-2-*ene*.—2 : 3-Epoxy-2 : 3-dimethylheptane (2 g.) gave 2 : 3-dimethylhept-2-ene (1·2 g.; b. p. 145—148°), b. p. on redistillation 145—146°, n_D^{24} 1·4300 (Found: C, 85·1; H, 14·7. Calc. for C_9H_{18}: C, 85·6; H, 14·4%). The physical properties agree with those reported by Levina *et al.*[42] but not with those given by Whitmore and Evers.[43] The b. p. observed by the American authors is lower than would be expected from comparison with analogous octenes.

Oct-3-*ene*.—3 : 4-Epoxyoctane (1·5 g.) was reduced in the usual manner, complete reduction at 5° needing about 2 hr. Oct-3-ene (0·9 g.; b. p. 122—124°) when redistilled had b. p. 122°, n_D^{22} 1·4122 (Found: C, 85·4; H, 14·1. Calc. for C_8H_{16}: C, 85·6; H, 14·4%). The infrared spectrum was that of a 1 : 1 mixture of *cis*- and *trans*-oct-3-ene.

3-*Methylpent*-2-*ene* (*Mixture of Geometrical Isomers*).—2 : 3-Epoxy-3-methylpentane (epoxide

[42] Levina, Fainsilberg, and Itenberg, *Doklady Akad. Nauk S.S.S.R.*, 1950, **75**, 39.
[43] Whitmore and Evers, *J. Amer. Chem. Soc.*, 1933, **55**, 814.

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α; 120 g.) was added during ½ hr. to an ice-cooled, stirred mixture of sodium iodide (130 g.), sodium acetate (30 g.), acetic acid (650 ml.), and zinc powder (200 g.). Stirring was continued for 2 hr. and the mixture was worked up as usual to give 3-methylpent-2-ene (76 g.), b. p. 66—70°. Redistillation followed by fractionation in a Podbielniak still separated it into approximately equal amounts of 3-methyl-*cis*- and -*trans*-pent-2-ene which were used to prepare the epoxides. The infrared spectrum of the total product was that of a 1 : 1 mixture of *cis*- and *trans*-isomers.

Stereospecific Reduction of 3 : 4-*Epoxyoctanes by Stannous Chloride–Hydrochloric Acid.*—*trans*-3 : 4-Epoxyoctane (1·5 g.) was added to a solution of sodium iodide (3 g.) in acetic acid (6 ml.) and water (0·5 ml.) at 5°. After 1 hr. the mixture was poured into water, and the iodohydrin was extracted with ether which was then washed with sodium hydrogen carbonate until neutral (a trace of sodium hydrogen sulphite removed free iodine), then with water, dried ($MgSO_4$), and evaporated at low pressure, leaving the nearly colourless iodohydrin (2·9 g.). This iodohydrin, when shaken with N-sodium hydroxide, reverted to an epoxide (1·15 g.; b. p. 49—50°/20 mm.) having an infrared spectrum identical with that of starting material.

The iodohydrin (from 1·28 g. of epoxide) was added to a solution of stannous chloride dihydrate (5 g.) in acetic acid (20 ml.) and hydrochloric acid (8 ml.; *d* 1·18). After 48 hr. the mixture was diluted with water and distilled. From the distillate the olefin (0·8 g.; b. p. 122—124°) was isolated as usual. The infrared spectrum was identical with that of *trans*-oct-3-ene. *cis*-3 : 4-Epoxyoctane (1·0 g.), similarly treated, gave a product (0·6 g.; b. p. 122—126°) having an infrared spectrum almost identical with that of *cis*-oct-3-ene (small C=O band).

The mixture of 3 : 4-epoxyoctanes from 3-chloro-octan-4-ol was reduced in the same way and gave a product having the infrared spectrum of a 7 : 3 mixture of *trans*- and *cis*-oct-3-ene.

Reduction of 2 : 3-*Epoxy*-3-*methylpentanes by Stannous Chloride–Hydrochloric Acid.*—*trans*-2 : 3-Epoxy-3-methylpentane (1 g.) was added to a solution of sodium iodide (2 g.) in acetic acid (6 ml.). After ½ hr. the mixture was added to stannous chloride dihydrate (6 g.) in hydrochloric acid (5 ml.; *d* 1·18) and acetic acid (25 ml.). The yield of olefin obtained after 24 hr. was 0·5 g. (b. p. 69—74°), and there was a higher-boiling fraction (up to 118°). The infrared spectrum of the olefin was that of a 7 : 3 mixture of 3-methyl-*trans*- and -*cis*-pent-2-ene. Reduction of *cis*-2 : 3-epoxy-3-methylpentane in the same way gave a similar yield of an olefin having the same composition. When the concentration of hydrochloric acid was lowered, less olefin and more higher-boiling ketone were formed. More ketone was also found with higher concentrations of hydrochloric acid. The ketonic material from several reactions was pooled; it boiled at 115—118°, and gave a 2 : 4-dinitrophenylhydrazone, m. p. 70°, and a semicarbazone, m. p. 95—96° (the corresponding figures for 3-methylpentan-2-one are 118°, 71·5°, 95°).

Either 3-methyl-*trans*-pent-2-ene or 3-methyl-*cis*-pent-2-ene was rapidly isomerised by stannous chloride–acetic acid–hydrochloric acid to a mixture (7 : 3-*trans* : *cis*) of both isomers. Stannous chloride in acetic acid alone caused very little change.

Stereospecific Reduction of Iodohydrins from cis- *and* trans-2 : 3-*Epoxy*-3-*methylpentane.*—*trans*-2 : 3-Epoxy-3-methylpentane (0·95 g.) was added to a cooled (−20°) solution of sodium iodide (2·5 g.) and sodium acetate (0·25 g.) in acetic acid (5 ml.) and propionic acid (10 ml.). After ½ hr. the mixture was warmed to room temperature and poured into ether and aqueous sodium hydrogen carbonate. The ether was washed with a little sodium hydrogen sulphite and with water, dried ($MgSO_4$), and evaporated at low pressure. The iodohydrin (1·86 g.) was added to a cooled (0°) solution of anhydrous stannous chloride (4 g.) in pyridine (15 ml.). Phosphoryl chloride (1 ml.) in pyridine (3 ml.) was then added with cooling. The mixture solidified after a few minutes. Next day water was added and the olefin was distilled. The distillate was neutralised (Methyl Orange) with sulphuric acid. The upper layer was then shaken with water and successive small quantities of solid iodine until persistence of colour showed that no phosphorus remained; it was then decolorised by sodium thiosulphate, dried (KOH), and distilled, to give 3-methyl-*trans*-pent-2-ene (0·5 g.), b. p. 70—72°. The infrared spectrum was identical with that of the pure *trans*-isomer separated by fractional distillation. *cis*-2 : 3-Epoxy-3-methylpentane (1·52 g.) was treated similarly, except that sodium iodide in acetic acid was used to prepare the iodohydrin. The product, 3-methyl-*cis*-pent-2-ene (0·66 g.), had b. p. 68—71° and its infrared spectrum was identical with that of the pure *cis*-isomer.

Stereospecific Reduction of Iodohydrin from 3 : 4-*Epoxyoctane.*—3 : 4-Epoxyoctane (1·5 g.; prepared from 3-chloro-octan-4-ol) was converted into the iodohydrin by treatment with sodium

iodide in acetic acid at 0°. The iodohydrin (3 g.) was added to an ice-cooled solution of anhydrous stannous chloride (4 g.) in pyridine (18 ml.). Phosphoryl chloride (1·2 ml.) in pyridine (4 ml.) was added slowly. Next day the oct-3-ene (1·15 g., 87%) was isolated as above; it had b. p. 122—124°. The infrared spectrum was identified with that of the product obtained by stannous chloride–hydrochloric acid.

Stereospecific Reduction of the Iodohydrin from 2 : 3-*Epoxy*-3-*methylheptane*.—The epoxide (1·5 g.) was added to a solution of sodium iodide (4 g.) and sodium acetate (0·5 g.) in acetic acid (8 ml.) and propionic acid (16 ml.) at −25°. After 3 hr. the mixture was poured into ether and aqueous sodium hydrogen carbonate, and the iodohydrin (2·9 g.) was isolated as usual. This was added to a cooled solution of anhydrous stannous chloride (3·5 g.) in pyridine (12 ml.) and treated with phosphoryl chloride (1·2 ml.) in pyridine (4 ml.) with ice-cooling. After 1 hr. water was added and the olefin, after removal of pyridine and phosphorus as before, was dried (KOH) and distilled (0·81 g.; b. p. 123—125°). Redistilled, the 3-methylhept-2-ene had b. p. 124—124·5°, n_D^{25} 1·4177. The infrared spectrum differed in small details from that of the previous specimen.

Stereospecific Reduction of the Iodohydrin from Epoxides α and β.—2 : 3-Epoxy-3-methylpentane α (22 g.) was added to a mixture of sodium iodide (45 g.), sodium acetate (4 g.), acetic acid (40 ml.), and propionic acid (100 ml.) at −30°. After ½ hr. at −30° to −20° the mixture was allowed to warm to 0° and after another ½ hr. it was poured into a mixture of ether and aqueous sodium hydrogen carbonate. The ether was washed with a little sodium hydrogen sulphite solution and with water, dried ($MgSO_4$), and evaporated at low pressure, leaving nearly colourless iodohydrin (49 g., 97%). An ice-cooled solution of anhydrous stannous chloride (70 g.) in pyridine (250 ml.) was added, then, cautiously during 5 min., phosphoryl chloride (18 ml.) in pyridine (50 ml.). The temperature was kept down by occasional cooling until the mixture solidified (10—15 min.). After 2 hr. water (300 ml.) was added and the mixture was worked up as above to give 3-methylpent-2-ene (15 g., 83% on iodohydrin), b. p. 66—70°. Redistilled through a short column it had b. p. 68—69° and the infrared spectrum was that of a mixture of 80—85% of 3-methyl-*cis*-pent-2-ene and 15—20% of 3-methyl-*trans*-pent-2-ene.

2 : 3-Epoxy-3-methylpentane β (40 g.) was treated similarly, to give 3-methylpent-2-ene (25·6 g.), b. p. 69—71°. On redistillation over sodium the b. p. was 69—70°/750 mm., and the infrared spectrum of the distillate was that of a mixture of 80—85% of 3-methyl-*trans*-pent-2-ene and 15—20% of 3-methyl-*cis*-pent-2-ene. Distillation of the two specimens of hydrocarbon in a Podbielniak still provided pure speciments of the *cis*- and *trans*-olefin and confirmed the proportions deduced from the infrared spectra.

3-*Methyl*-cis-*pent*-3-*eno*-5-*lactone and* 5-*Hydroxy*-3-*methyl*-trans-*pent*-3-*enoic Acid*.—The preparation of these substances on a small scale has already been described.[30] Methyl vinyl ketone (43 g.) and methyl bromoacetate (85 g.) were dissolved in dry benzene (212 ml.) and 60 ml. of this solution added to activated zinc wool (45 g.) and mercuric chloride (0·4 g.) in benzene (212 ml.). The mixture was refluxed and stirred (bath 85—90°) until vigorous reaction set in (10 min.), then the remainder of the benzene solution was added at a rate which maintained vigorous refluxing (bath at 85°; 30 min.). The mixture was stirred and refluxed for 1 hr. longer, cooled, decomposed by acetic acid (41 ml.) in water (350 ml.), and worked up in the normal manner to give methyl 3-hydroxy-3-methylpent-4-enoate (47·7 g., 60% on methyl bromoacetate), b. p. 66—68°/13·5 mm. This ester (168·8 g.) was converted in two portions as previously described [30] into methyl 5-bromo-3-methylpent-3-enoate; each batch of crude bromide was shaken for 2½ days in dry acetone (2 l.) with anhydrous potassium acetate (330 g.). After filtration and evaporation the combined products were distilled, to give methyl 3-methylpenta-2 : 4-dienoate (53·9 g.) and methyl 5-acetoxy-3-methylpent-3-enoate (79·9 g.). The acetoxy-ester (75 g.) was dissolved in 0·1N-sodium hydroxide (9 l.); next day the neutralised (Phenol Red) solution was evaporated at low pressure, acidified, and extracted with ether. The product on distillation gave crude 3-methyl-*cis*-pent-3-eno-5-lactone (13·9 g.) and 5-hydroxy-3-methylpent-3-enoic acid (10·4 g.). The lactone was purified by washing it in ether with aqueous sodium hydrogen carbonate and redistilling it (b. p. 112°/14 mm.; 8·0 g.). The *trans*-hydroxy-acid was recrystallised from dry ether at −70° to give 8·75 g. of material having m. p. 48—52°. A further quantity (6·8 g.) of the *trans*-hydroxy-acid was obtained by hydrolysing the residue from distillation, which presumably contained polyester. *Methyl* 5-*hydroxy*-3-*methyl*-trans-*pent*-3-*enoate*, prepared by means of diazomethane, had b. p. 72—73°/0·2 mm. (Found: C, 58·5; H, 8·4. $C_7H_{12}O_3$ requires C, 58·3; H, 8·3%).

XUM

3-*Methyl*-cis-*pent*-2-*ene*-1 : 5-*diol*.—Lithium aluminium hydride (2·7 g.) in ether (100 ml.) was stirred overnight and cooled to −15°. 3-Methyl-*cis*-pent-3-eno-5-lactone (8·0 g.) in ether (50 ml.) was added during ½ hr. After a further 2·5 hr. ethyl acetate (10 ml.) in ether (20 ml.) was added, and then saturated aqueous ammonium chloride (20 ml.). The residue after filtration was extracted with hot methanol which was then evaporated, and the residue was extracted with ether. The combined ethereal solutions were distilled, giving 3-*methyl*-cis-*pent*-2-*ene*-1 : 5-*diol* (XXXII; X = OH), b. p. 98°/0·6 mm., n_D^{20} 1·4810 (6·7 g., 80%) (Found: C, 62·2; H, 10·3. $C_6H_{12}O_2$ requires C, 62·1; H, 10·3%). The same diol was obtained by reduction of 3-methyl-*cis*-pent-2-eno-5-lactone.[30] The *di*-p-*nitrobenzoate* crystallised from butan-1-ol in colourless rosettes, m. p. 126—127° (Found: C, 57·6; H, 4·3; N, 6·4. $C_{20}H_{18}O_8N_2$ requires C, 58·0; H, 4·3; N, 6·7%).

3-*Methyl*-trans-*pent*-2-*ene*-1 : 5-*diol*.—Reduction of the *trans*-hydroxy-acid (XXIX) and of its methyl ester by lithium aluminium hydride in ether was incomplete. Methyl 5-hydroxy-3-methyl-*trans*-pent-3-enoate (3·3 g.; recovered from attempted reduction in ether) was added to a mixture of lithium aluminium hydride (3 g.) and tetrahydrofuran (60 ml.) which had previously been stirred under reflux for 1 hr. The complex which first separated dissolved overnight. After decomposition with ethyl acetate (18 ml.) and ammonium chloride solution (17 ml.) the mixture was worked up as with the *cis*-diol to give the trans-*diol* (XXXI; X = OH) (1·9 g.), b. p. 100—102°/0·2 mm. (Found: C, 62·2; H, 10·3%). The *di*-p-*nitrobenzoate* crystallised from butan-1-ol in colourless needles, m. p. 104° (Found: C, 57·6; H, 4·4; N, 7·1%).

1 : 5-*Dibromo*-3-*methyl*-cis-*pent*-2-*ene*.—Triphenyl phosphite benzylobromide was best prepared (cf. Harrison and Lythgoe [31]) by heating together benzyl bromide and triphenyl phosphite (4% excess) under nitrogen with exclusion of moisture for 72 hr. at 130—140°. The glassy product was dissolved in warm tetrahydrofuran and the slurry of hygroscopic crystals obtained on cooling was used for reaction with the alcohols.

3-Methyl-*cis*-pent-2-ene-1 : 5-diol (3·5 g.) in tetrahydrofuran (4 ml.) was added to the benzylobromide (50% excess) in tetrahydrofuran. The mixture became warm and the solid largely dissolved. Next day the solvent was removed at low pressure and the residue extracted five times with light petroleum (b. p. 40—60°), which was then shaken with ice-cold 0·5N-sodium hydroxide (5 × 50 ml.), filtered, dried, and evaporated at low pressure. The residue, after two distillations, gave 1 : 5-*dibromo*-3-*methyl*-cis-*pent*-2-*ene* (XXXII; X = Br) (7·01 g., 97%), b. p. 42—46°/0·005 mm. (Found: C, 29·5; H, 4·2; Br, 66·4. $C_6H_{10}Br_2$ requires C, 29·8; H, 4·1; Br, 66·1%).

1 : 5-*Dibromo*-3-*methyl*-trans-*pent*-2-*ene*.—The *trans*-diol (3·3 g.), treated as above, gave 1 : 5-*dibromo*-3-*methyl*-trans-*pent*-2-*ene* (XXXI; X = Br) (5·9 g.), b. p. 46°/0·005 mm. (Found: C, 29·9; H, 4·2; Br, 66·3%).

3-*Methyl*-cis- *and* -trans-*pent*-2-*ene*.—Two reductions of 1 : 5-dibromo-3-methyl-*cis*-pent-2-ene by lithium aluminium hydride in dibutyl ether at 70° were carried out with very poor results; from the dibromide (11·8 g.) a product (1·0 g.; b. p. 67—69°), smelling strongly of butyraldehyde, was obtained. This was shaken with aqueous semicarbazide acetate, washed with water and aqueous sodium hydrogen carbonate, dried ($CaSO_4$), and distilled, to give 3-methyl-*cis*-pent-2-ene (366 mg.), b. p. 69° (Found: C, 85·4; H, 14·8%).

A somewhat better result was then achieved with the *trans*-dibromide. Lithium aluminium hydride (2·5 g.) in dibutyl ether (80 ml.; freed from peroxide by passage through a column of alumina) was stirred for 4 hr. at 70°. 1 : 5-Dibromo-3-methyl-*trans*-pent-2-ene (5·7 g.) was added during 30 min. and the mixture was stirred at 70° for a further 1 hr., a test then showing little remaining organic halide. The mixture was cooled to −15° and water (12 ml.) was cautiously added. After filtration and washing of the residue with dibutyl ether the ethereal solution was distilled through a column. The distillate, b. p. 140°, was treated as above with semicarbazide and refractionated, to give 3-methyl-*trans*-pent-2-ene (702 mg.); b. p. 70—72° (Found: C, 85·2; H, 14·8%).

We suspect that the low yields in these reductions are due to some fission of dibutyl ether by lithium aluminium hydride, to give lithium butoxide which can react with some of the bromide to give a high-boiling ether and the trace of $C{=}CH_2$ (diene?) indicated by the infrared spectra of the *cis*-pentene.

3-*Chloro*-*octan*-4-*one*.—3-Chloro-octan-4-ol (5 g.) in benzene (50 ml.), and chromium trioxide (6 g.) in water (15 ml.), were cooled in water and stirred during addition (30 min.) of sulphuric acid (7 ml.; *d* 1·84) in water (7 ml.). After 4½ hr. water was added and the benzene layer was

washed with aqueous sodium hydrogen carbonate and with water, dried ($CaCl_2$), and distilled, to give **3-*chloro-octan*-4-*one*** (4·1 g.); b. p. 83—85°/16 mm. (no infrared hydroxyl band was found) (Found: C, 58·7; H, 9·1. $C_8H_{15}OCl$ requires C, 59·1; H, 9·2%).

Reduction of 3-*Chloro-octan*-4-*one*.—The chloro-ketone (3·25 g.) in ethanol (20 ml.) was mixed with sodium hydrogen carbonate (2 g.) in water (20 ml.), and sodium borohydride (0·38 g.) in water (10 ml.) was added. After ½ hr. water and dilute sulphuric acid were added, and the product was isolated by extraction with ether and distillation. The **3-*chloro-octan*-4-*ol*** (2·95 g.) had b. p. 95—97°/18 mm. and no infrared carbonyl band (Found: C, 58·4; H, 10·5. $C_8H_{17}OCl$ requires C, 58·3; H, 10·4%). The chlorohydrin (2·8 g.) was converted as described earlier into 3 : 4-epoxyoctane (1·7 g.; b. p. 54—55°/25 mm.), which was shown by infrared analysis to be a mixture of 80—85% of *cis*-3 : 4-epoxyoctane and 15—20% of *trans*-3 : 4-epoxyoctane. Reduction by the stereospecific procedure described above gave a mixture of 80—85% of *cis*- and 15—20% of *trans*-oct-3-ene.

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25. *Spectrophotometric Determination of the Acid Dissociation Constants of Hydrogen Sulphide.*

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The first acid dissociation constant of hydrogen sulphide has been found by spectrophotometry to be $9·5 \times 10^{-8}$ at 25°, and the second to be $1·0 \times 10^{-14}$ at 20°. The method was based on the fact that HS^- ions absorb strongly at 2300 Å, whereas for H_2S molecules and S^{2-} ions the absorption is much less. The logarithm of the molar extinction coefficient at 2300 Å for HS^- ions is $3·90 \pm 0·01$.

VALUES in the literature for both the first (K_1) and the second (K_2) acid dissociation constant of hydrogen sulphide are not in good agreement. As the HS^- ion absorbs strongly in the ultraviolet region at 2300 Å [1,2] Robinson and Biggs's method [3] for determining the dissociation constants of weak acids and bases can be applied.

The first thermodynamic dissociation constant is given by $K_1 = a_H\gamma_{HS}\alpha/(1 - \alpha)$, where a_H is the hydrogen-ion activity, α is the fraction of sulphide present as HS^- (at pH's where the S^{2-} ion concentration can be neglected), and γ_{HS} is the activity coefficient of this ion. The activity coefficient of the H_2S molecules is assumed to be unity at the concentrations used. The degree of dissociation, α, was obtained from measurements of the molal extinction coefficient of hydrogen sulphide in buffered solutions (pH 6·5—7·2), in acid solutions (pH 1·0—3·0), and in solutions at pH 10·5.

Buffers of known hydrogen-ion activity [4,5] were used at various ionic strengths. At each, γ_{HS} was calculated by the equation suggested by Davies,[6] $-\log\gamma = [0·5\,\mu^{\frac{1}{2}}/(1 + \mu^{\frac{1}{2}})] - 0·1\mu$, and a value of K_1 obtained. The values of K_1 showed little significant variation with ionic strengths between 0·01 and 0·4.

The second dissociation constant can be expressed by the equation $K_2 = a_H\gamma_S\alpha'/(1 - \alpha')\gamma_{HS} = K_w\gamma_S\alpha'/(1 - \alpha')m_{OH}\gamma_{OH}\gamma_{HS}$, where K_w is the thermodynamic dissociation constant of water, γ_S and γ_{OH} the activity coefficients of the S^{2-} ions and the

[1] Noda, Kuby, and Lardy, *J. Amer. Chem. Soc.*, 1953, **75**, 913.
[2] Orgel, *Quart. Reviews*, 1954, **8**, 428.
[3] Robinson and Biggs, *Trans. Faraday Soc.*, 1955, **51**, 901.
[4] Bates and Acree, *J. Res. Nat. Bur. Stand.*, 1943, **30**, 129.
[5] *Idem, ibid.*, 1945, **34**, 373.
[6] Davies, *J.*, 1938, 2093.

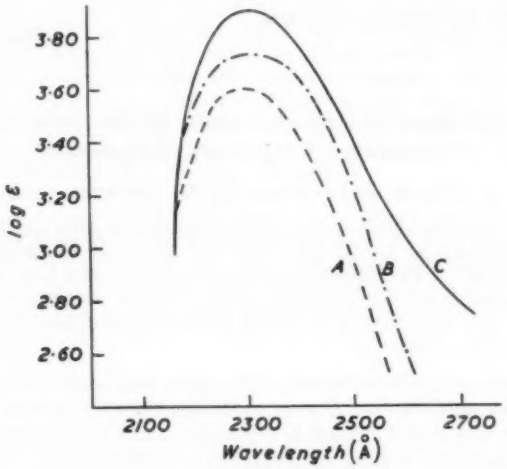
OH^- ions respectively, and m_{OH} the molality of hydroxide. α' is the fraction of sulphide present as S^{2-} in alkaline solutions where the H_2S concentration can be neglected.

As K_2 is of the order of 10^{-14}, measurements must be made in strongly alkaline solutions for the fraction of S^{2-} ions to be appreciable. Solutions of lithium, sodium, and potassium hydroxides were used at concentrations ranging from 0·25 to 2·5 molal, and values of K_2' obtained by assuming the activity-coefficient ratio $\gamma_S/(\gamma_{OH}\gamma_{HS})$ to be unity. It is not possible to calculate the true value for this ratio, but from the trend of K_2' with hydroxide concentration a useful approximation for the thermodynamic dissociation constant K_2 can be obtained.

Experimental

Methods and Materials.—Absorption spectra were measured with a Beckman model DU spectrophotometer in a room maintained at constant temperature. Matched fused silica cells with a 1 cm. light-path were used.

In the experiments for determining K_2, standardised carbonate-free lithium hydroxide, sodium hydroxide, and potassium hydroxide solutions were used to control the alkalinity.



Hydrogen sulphide was prepared by treating "AnalaR" sodium sulphide with dilute sulphuric acid. Precautions against oxidation of the solutions by the atmosphere were unnecessary at neutral pH's, but the alkaline solutions were prepared in oxygen-free water, and transferred in a nitrogen atmosphere. Oxidation of hydrogen sulphide by the air occurs much more rapidly in alkaline solutions.

Concentrations were estimated by adding a known weight of sulphide solution to acidified iodine, and back-titrating the excess of iodine with standard thiosulphate.

The absorption of the HS^- ion at 2300 Å in borate buffers obeys Beer's law, and from the slope of the absorption *versus* concentration graph the logarithm of the molar extinction coefficient (log ε) is 3·90 $\pm$ 0·01. This average represents twenty results on sulphide solutions ranging from 10^{-6} to 3×10^{-4}M. For comparison, the values reported by Orgel [3] and by Noda, Kuby, and Lardy [1] are 3·68 and 3·88 respectively.

In the Figure log ε is plotted against wavelength for hydrogen sulphide in M- (*A*) and 0·5M- (*B*) sodium hydroxide solutions, and in a borate buffer (*C*) of pH 11·15. At high alkalinities no peak or inflection in the curves appears which would correspond to the absorption of the S^{2-} ion. For molecular hydrogen sulphide in a 0·01N-hydrochloric acid solution log ε is 1·49 at 2300 Å.

In these tables, *D* is the observed optical density of the solutions at 2300 Å. α is obtained from *D* and the known absorption of the HS ions and hydrogen sulphide molecules. The pH of the buffers ($-\log m_H\gamma_H$ from Bates and Acree's data [4,5]) is altered slightly by the addition of

hydrogen sulphide. Column 6 shows the pH of the solutions corrected for this effect by Robinson and Biggs's method.[3]

TABLE 1. *Results for K_1 by use of phosphate buffers*[4] *at* 25° ± 1° *containing* $(KH_2PO_4) : (Na_2HPO_4) : (NaCl) = 1 : 1{\cdot}529 : 1$ molar.

$\mu^{\frac{1}{2}}$	D	Total H_2S (10^4m)	α	Buffer pH	Corrected pH	$-\log \gamma_{HS}$	pK_1
0·412	0·876	2·03	0·542	6·966	6·962	0·129	7·02
0·281	0·867	1·88	0·579	7·064	7·057	0·101	7·02
0·228	0·614	1·30	0·595	7·110	7·105	0·088	7·03
0·139	1·045	2·14	0·613	7·202	7·171	0·059	7·03
0·113	1·12	2·29	0·613	7·229	7·180	0·049	7·03

TABLE 2. *Results for K_1 by use of phosphate buffers*[4] *at* 25° ± 1° *containing* $(KH_2PO_4) : (Na_2HPO_4) : (NaCl) = 1 : 0{\cdot}6376 : 1$ molar.

$\mu^{\frac{1}{2}}$	D	Total H_2S (10^4m)	α	Buffer pH	Corrected pH	$-\log \gamma_{HS}$	pK_1
0·449	0·565	2·18	0·323	6·564	6·562	0·135	7·02
0·336	0·719	2·55	0·351	6·640	6·637	0·114	7·02
0·192	0·872	2·79	0·391	6·766	6·753	0·077	7·02
0·127	0·680	2·06	0·413	6·835	6·814	0·055	7·02
0·105	1·15	3·52	0·408	6·860	6·809	0·046	7·02

TABLE 3. *Results for K_1 by use of phosphate buffers*[5] *at* 25° ± 1° *containing equimolar* KH_2PO_4 *and* Na_2HPO_4, *and no sodium chloride.*

$\mu^{\frac{1}{2}}$	D	Total H_2S (10^4m)	α	Buffer pH	Corrected pH	$-\log \gamma_{HS}$	pK_1
0·633	1·06	3·34	0·395	6·671	6·669	0·154	7·01
0·447	0·890	2·57	0·433	6·772	6·770	0·135	7·02
0·316	0·790	2·10	0·471	6·860	6·856	0·110	7·02
0·200	0·410	1·01	0·506	6·959	6·955	0·079	7·02
0·141	0·910	2·19	0·520	7·018	6·999	0·060	7·02

From the three series of results the average value for pK_1 is 7·02.

TABLE 4. *The second acid dissociation constant of hydrogen sulphide at* 20°.

NaOH Solutions					LiOH Solutions	
Alkali concn. (m) ...	2·46	1·00	0·50	0·25	Alkali concn. (m)	1·00
pK_2'	14·00	13·96	13·97	13·96	pK_2'	13·89
$\gamma_{\pm\,(NaOH)}$	0·709	0·678	0·690	0·716	$\gamma_{\pm\,(LiOH)}$	0·554
KOH Solutions						
Alkali concn. (m) ...	5·00	2·00	1·00	0·50	0·25	
pK_2'	14·8	14·01	13·83	13·81	13·91	
$\gamma_{\pm\,(KOH)}$	1·72	0·888	0·756	0·732	0·749	

Table 4 gives the values obtained for $K_2' = K_w\alpha'/(1 - \alpha')m_{OH}$ in different alkali solutions. Each value of pK_2' is derived from a series of approximately six experiments in the particular alkali solution. In each series the HS^- concentrations found from the optical absorption of the solutions at 2300 Å were plotted against the total sulphide concentrations found by iodine titration. The fraction $\alpha'/(1 - \alpha')$, and hence the average pK_2, was obtained from the slope of this graph. The total sulphide concentrations used in these experiments were in the range 5×10^{-5} to 7×10^{-4}m.

The variations in the mean activity coefficients, $\gamma_\pm$, of the pure alkali hydroxide solutions, as reported by Robinson and Stokes,[7] are given for comparison in Table 4. The values of pK_2 from sodium and potassium hydroxide solutions show a trend with concentration similar to the values of $\gamma_\pm$ for the particular alkali solution. Extrapolation of graphs of pK_2 *versus* alkali concentration from 0·25m to zero ionic strength, where $\gamma_S/\gamma_{HS}\gamma_{OH} = 1$, gives a value of pK_2 of 14·00.

[7] Robinson and Stokes, "Electrolyte Solutions," Butterworths Scientific Publications, London, 1955.

TABLE 5. *Acid dissociation constants of hydrogen sulphide.*

Source	Method	10^7K_1	$10^{14}K_2$	Temp.
This work	Spectrophotometric	0·95	—	25°
,,	,,	—	1·0	20
Kubli [a]	Potentiometric	0·873	36·3	,,
Epprecht [b]	,,	3·31	—	18
Yui [c]	,,	1·24	—	25
Knox [d]	Hydrolysis	—	0·12	18
Kuster and Heberlein [e]	,,	—	6·0	,,
Auerbach [f]	Conductance	0·91	—	,,
Walker and Cormack [g]	,,	0·57	—	,,
Konopik and Leberl [h]	Colorimetric pH	—	7·9	20

[a] Kubli, *Helv. Chim. Acta*, 1946, **29**, 1962. [b] Epprecht, *ibid.*, 1938, **21**, 205. [c] Yui, *Sci. Rep. Tohoku Univ.*, 1951, **35**, 53. [d] Knox, *Z. Elektrochem.*, 1906, **12**, 477. [e] Kuster and Heberlein, *Z. anorg. Chem.*, 1905, **43**, 53. [f] Auerbach, *Z. physikal. Chem.*, 1904, **49**, 220. [g] Walker and Cormack, *J.*, 1900, **77**, 5. [h] Konopik and Leberl, *Monatsh.*, 1949, **80**, 781.

Table 5 gives for comparison some of the values reported previously for K_1 and K_2. The discrepancies in values of K_2 possibly arise from the instability of alkaline sulphide solutions in air. Although it is unlikely that the present value presented for K_2 is more accurate than $\pm 20\%$, this is a distinct improvement over the uncertainties which existed previously.

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26. *Picrotoxin and Tutin. Part IX.**

By R. M. CARMAN, GHULAM HASSAN, and R. B. JOHNS.

Evidence is presented which establishes the relative positions of the carboxylic acid, lactone, and secondary hydroxyl groups, and one point of attachment of the ether linkage, and the potential α-glycol unit in β-bromopicrotoxinic and α-picrotoxinic acid. These results confirm substantially Conroy's structure for picrotoxinin.

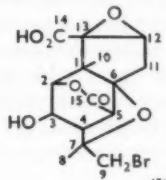
IN recent papers,[1] plausible structures based on mechanistic and stereochemical arguments have been presented for picrotoxinin and its more important derivatives. Nevertheless, the evidence for the contentious aspect of picrotoxinin chemistry, *viz.*, the function and position of the ether-oxygen link, is still indirect rather than positive. Before our recent publication [2] there had been no confirmation of the relative position of any of the oxygen atoms within the molecule as the result of stepwise degradation. This paper describes further experiments of this nature which also have a direct bearing on the position of the ether function in picrotoxinin.

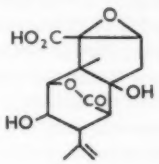
β-Bromopicrotoxinic acid is formed from β-bromopicrotoxinin under alkaline conditions by the irreversible opening of one lactone ring to give the carboxylic acid, together with a change of the remaining lactone from a five- to a six-membered system.[1] One hydroxyl group only is present in β-bromopicrotoxinic acid [1] and by oxidation with chromic acid in acetic acid [3] or, better, in acetone the corresponding keto-acid, showing no infrared hydroxyl absorption, is obtained in good yield. Conroy [1] has formulated β-bromopicrotoxinic acid and the reversibly related α-picrotoxinic acid as (I) and (II) respectively, the evidence being largely spectral and stereochemical; the position of the epoxide ring is the result of arguments of elimination rather than otherwise.

* Part VIII, *J.*, 1956, 4715.

[1] *E.g.*, Conroy, *J. Amer. Chem. Soc.*, 1957, **79**, 1726.
[2] Johns, Woods, and Slater, *J.*, 1956, 4715.
[3] Sutter and Schlittler, *Helv. Chim. Acta*, 1950, **33**, 902.

Reduction [2] of β-bromopicrotoxinic acid with lithium aluminium hydride, followed by oxidation with periodate, giving a small-ring cyclic ketone and formaldehyde, suggests that the lactone giving rise to the carboxyl group is that shown in (I), and experiments with Grignard reagents on methyl β-bromopicrotoxinate, discussed more fully below, confirm


(I)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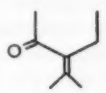
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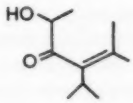

(IV)

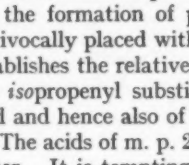
our result. In agreement with Conroy,[4] we find that β-bromopicrotoxinic acid is recovered after treatment with lead tetra-acetate and consequently the hydroxyl group cannot be in an α-position to the carboxyl group. The retention of the ether linkage in both acids (I) and (II), on the basis of the available chemical evidence bearing directly on the functional groups of these compounds, seems reasonable. Debromination of oxo-β-bromopicrotoxinic acid, $C_{15}H_{15}O_7Br$, leads to the expected product, $C_{15}H_{16}O_7$, m. p. 219°, which, like α-picrotoxinic acid, is unstable to warm alkali, together with an alkali-stable acid, $C_{15}H_{18}O_8$, m. p. 251°. The acid of m. p. 219° shows infrared maxima 1764 cm.$^{-1}$ (lactone), 1732 cm.$^{-1}$ (CO_2H), 1708 and 1615 cm.$^{-1}$ (unsaturated ketone) and ultraviolet maxima at 260 and 340 mμ consistent with the presence of a fully substituted αβ-unsaturated ketone with the double bond exocyclic to the six-membered ring. These facts, together with the formation of acetone by ozonolysis, enable us partially to formulate the acid as (III).

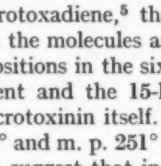
The acid of m. p. 251° also showed light absorption typical of an αβ-unsaturated ketone (1745 cm.$^{-1}$, lactone), (1712 cm.$^{-1}$, CO_2H), (1675 and 1600 cm.$^{-1}$, unsaturated ketone). Ultraviolet maxima at 247 and 318 mμ are consistent with an endocyclic double bond and this is confirmed by the fact that no volatile product could be detected on ozonolysis. The higher-melting acid could be obtained from the lower-melting one in good yield under the usual conditions of debromination. The acid of m. p. 251° possesses reducing properties but is alkali-stable, a distinction from the acid of m. p. 219°, and, whilst the latter is stable to periodic acid, the former reacts with uptake of one equivalent. Disappearance of maxima associated with the αβ-unsaturated ketone in the infrared and the ultraviolet spectrum of the periodate product, isolated as the 2 : 4-dinitrophenylhydrazone, indicates periodate fission of the original acid to have involved the carbonyl group. This fact, taken in conjunction with its reducing properties, allows a partial formulation (IV) to be advanced for the acid, m. p. 251°; *i.e.*, it is an α-ketol. The hydrazone, $C_{21}H_{20}O_{11}N_4$, contains a molecule of water less than would be expected. It is probable that lactonisation with a suitably placed hydroxyl group has occurred, removing the carboxyl function generated by the periodate oxidation. (This is supported by the appearance of infrared bands at 1775 and 1725 cm.$^{-1}$.) The double bond in the acid, m. p. 219°, exocyclic to the six-membered ring establishes the position of the carbonyl group, and hence the secondary hydroxyl group at position 3 in both β-bromopicrotoxinic and α-picrotoxinic acid. Likewise the formation of an α-ketol confirms the presence of a further oxygen atom at position 2. (These two oxygen atoms presumably form the glycol system in picrotoxinindicarboxylic acid.) That this second oxygen atom is a potential hydroxyl group in the acid derivatives under discussion is clear from a consideration of the relation between the acids of m. p. 251° and 219°. In the bromopicrotoxinic acids, α-picrotoxinic acid, and the unsaturated ketonic acids the same lactone gives rise to the carboxyl function. From published evidence,[2] supported by further work described below, this is the 14-carbonyl group. In the acid of m. p. 251°, however, the δ-lactone has isomerised (the 1764 cm.$^{-1}$ lactone band

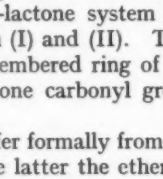
[4] Conroy, *Chem. and Ind.*, 1957, 704.

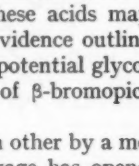
in the acid of lower m. p. has been replaced by one at 1745 cm.$^{-1}$) and from stereochemical considerations of a system containing an endocyclic double bond, as in (IV), lactonisation between the 15-carbonyl and a 2-hydroxyl group is unlikely. Simultaneous formation of the α-ketol and isomerisation of the δ-lactone strongly suggests that it is this 2-hydroxyl group in β-bromopicrotoxinic acid which is free in the acid, m. p. 251°, and bound in the lactone systems of the acid, m. p. 219°, and α-picrotoxinic and β-bromopicrotoxinic acid. If this view is accepted and considered in conjunction with the carbon skeleton established by the formation of picrotoxadiene,[5] the δ-lactone system in these acids may be unequivocally placed within the molecules as in (I) and (II). The evidence outlined above establishes the relative positions in the six-membered ring of the potential glycol system, the *iso*propenyl substituent and the 15-lactone carbonyl group of β-bromopicrotoxinic acid and hence also of picrotoxinin itself.

The acids of m. p. 219° and m. p. 251° differ formally from each other by a molecule of water. It is tempting to suggest that in the latter the ether linkage has opened and a


(V)


(VI)


(VII)


(VIII)

relactonisation occurred to form (V) (on the basis of Conroy's structure for picrotoxinin); the acid of m. p. 219° would then be (VI). The position of the lactone in (V) is similar to that proposed by Conroy for *apo*picrotoxinic dilactone.[1] Like this compound, after treatment with alkali, the acid (V) reacted with two equivalents of periodic acid, which is consistent with the view that in the corresponding diacid there is a glycol unit in addition to the original α-ketol system.

Grignard reagents may react with epoxides [6] in the manner: $\rangle C\!-\!C\langle + RMgX \longrightarrow \rangle C(OMgX)\cdot CR\langle$. The advantages of labelling one point of attachment with an alkyl radical are obvious, and in the hope of providing positive evidence for the presence and position of the oxiran ring methyl β-bromopicrotoxinate was treated with methylmagnesium iodide. The major product, $C_{18}H_{27}O_6Br$, showed only hydroxyl absorption in the infrared spectrum and formed a monoacetate which still had maxima in the hydroxyl region. The compound itself reacted cleanly with one equivalent of periodate under acidic or slightly basic conditions and with neutral lead tetra-acetate to give in good yield a product, $C_{15}H_{19}O_5Br$, possessing infrared (1767 cm.$^{-1}$) and ultraviolet (301 mμ) absorption maxima consistent with the presence of a five-membered ring ketone, together with acetone isolated in high yield as its 2 : 4-dinitrophenylhydrazone. This confirms the view [2] that it is the 14-carbonyl group of picrotoxinin which in β-bromopicrotoxinic and related acids is present as the carboxyl function. The ketone was unchanged by further treatment with periodate, did not form a benzylidene derivative under the usual conditions, and was recovered after treatment with selenium dioxide. From this it may be concluded that there is no methylene group α to the carbonyl function.

The formation of a mol. of acetone at varying pH's can occur only if in the Grignard product there is an actual, rather than a potential, hydroxyl group at position 13. The reaction of the methoxycarbonyl group to give the grouping $Me_2C(OH)\cdot C(OH)\langle$ necessary

[5] *Idem, J. Amer. Chem. Soc.*, 1952, **74**, 491.
[6] Kharasch and Reinmuth, "Grignard Reactions of Non-metallic Substances," Prentice-Hall, New York, 1954, p. 961.

for the formation of acetone accounts for two of the three molecules of methane formally added to the original molecule. The remaining equivalent must have reacted with the lactone-carbonyl group since the infrared spectrum of the product showed no absorption in this region. Similarly, because of the absence of hydroxyl absorption in the spectrum of the monoacetate of the cyclic ketone, in which the 3-hydroxyl group is acetylated, the Grignard reagent could not have formed the expected hemiketal. The original lactone system, however, must remain essentially unchanged since there is no free 2-hydroxyl group. These facts are explained by assuming that a ketal rather than a hemiketal group has been generated, but such a system requires the presence in the molecule of a new ether linkage. The formation of a 13-hydroxyl group, reaction of the 15-lactone carbonyl group to give a ketal, and the presence of a substituted methylene group α to the cyclic ketone, find a plausible explanation on the basis of the opening of an oxiran ring in the manner postulated by Conroy [1] to account for the reduction with sodium borohydride of β-bromopicrotoxinic acid and accepted by Robertson [7] to account for the products of reduction of picrotoxinin by lithium aluminium hydride. These considerations provide important, but only indirect, evidence, for the position and function of the ether linkage. The Grignard product may accordingly be formulated as (VII) and the ketone as (VIII; R = Me, R′ = OH).

β-Bromopicrotoxinic acid with methylmagnesium iodide gives results similar to those described for the methyl ester. The only product, isolated in small yield, was a compound $C_{16}H_{21}O_7Br$. Its stability to periodic acid but ready oxidation with lead tetra-acetate to a cyclic ketone, identical with that obtained *via* the methyl ester, shows that the Grignard attack on the lactone had given rise to a 15-ketal and a 13-hydroxyl group. From these results we may conclude that in β-bromopicrotoxinic acid, in its methyl ester, and hence in picrotoxinin itself, there is an oxygen atom present in some ether function, of which one point of attachment is position 13.

Positive evidence for an oxygen attachment at position 12 would be obtained if the ketal group in (VIII; R = Me, R′ = OH) could be opened to give an α-ketol. Attempts to bring about partial or complete fission under a variety of conditions gave unchanged ketone or intractable oils. It is probable that the stereochemical requirements of the oxygen bridge formed during bromination preclude a simple opening of the ketal under the conditions used. A comparison of the carbonyl absorptions of the various ketones described in this paper (see Table) emphasises the considerable steric strain and molecular rigidity inherent in the brominated structures. Both the infrared and the ultraviolet

	Light absorption maxima		
		Infrared (cm.$^{-1}$)	
Substance	Ultraviolet (mμ)	Six-membered	Five-membered
β-Bromo-oxopicrotoxinic acid	316	1744	—
β-Bromopicrotoxinic acid + $LiAlH_4$ + HIO_4 [1]	302—305	—	1768
Acetate of above ketone [2]	—	—	1762
Methyl-β-bromopicrotoxinate + MeMgI + HIO_4	301	—	1767
Methyl-β-bromopicrotoxinate + MeMgI + HIO_4 + CrO_3	316	1749	1769
2 : 4-DNP of diketone above	—	1749	—
β-Bromopicrotoxinic acid + $LiAlH_4$ + HIO_4 debrominated	301—302	—	1753
Me_2 picrotoxinin dicarboxylate + CrO_3 [2] *	299	1699	—

[1] Part VIII, *J.*, 1956, 4715. [2] Carman, Johns, and Slater, unpublished work. * This is an α-hydroxy-ketone, which would account for a further small shift of the absorption maximum.

absorption maxima, although self-consistent, are considerably displaced from the range in which five- or six-membered ring ketones normally absorb. Consistent with this view is the return to lower frequencies in the debromination products or in structures such as picrotoxinindicarboxylic acid. Accordingly, debromination of the ketone was attempted, but owing to the small yield this approach was abandoned in favour of the debromination

[7] Holker, Holker, McGookin, Robertson, Sargeant, and Hathway, *J.*, 1957, 3746.

XUM

of the related ketone (VIII; R = H, R′ = OH) obtained by reduction of methyl β-bromopicrotoxinate with lithium aluminium hydride and subsequent treatment with periodate. This route gave a 25% yield of the desired compound which reacted with 0·5 mol. of periodic acid at room temperature in 24 hours, a result which could be explained by partial hydrolysis of the acetal under acid conditions.

Oxidation of the alcohol (VII) under acid conditions with chromic oxide in acetone [8] proved complex. The major product was a diketone $C_{15}H_{17}O_5Br$, also obtained from the monoketone (VIII; R = Me, R′ = OH) by further oxidation. Absorption in the infrared (1769 and 1749 cm.$^{-1}$) and the ultraviolet (316 mμ) region suggests that both five- and six-membered ring ketone groupings are present in the molecule, hence it is formulated as (VIII; R = Me, R′ = O). Two further ketones, whose analyses best fit formulæ $C_{17}H_{21}O_7Br$ (C:O absorption at 1741 cm.$^{-1}$ and 315 mμ; presumably six-membered ring) and $C_{18}H_{25}O_6Br$ (max. at 1755, 1732, and 1701 cm.$^{-1}$; 299 mμ), were also isolated. In both cases the poor yield precluded close investigation. Further experiments, which it is hoped will elucidate the nature of the substitution on the three remaining carbon atoms $C_{(6)}$, $C_{(11)}$, and $C_{(12)}$, are in progress.

Experimental

Oxidation of β-Bromopicrotoxinic Acid.—A solution of β-bromopicrotoxinic acid (1 g.) in acetone (3 ml.) was treated at <10° with an excess of a solution of chromic acid [8] (5 ml.) and kept overnight at room temperature, then diluted with water (100 ml.) and kept in a refrigerator for 4 hr. *β-Bromo-oxopicrotoxinic acid* crystallised (0·9 g.). Recrystallised from ethanol it had m. p. 173—174° (Found: C, 45·7; H, 4·1. $C_{15}H_{15}O_7Br$ requires C, 46·4; H, 4·1%). The ketone reduced Tollens's reagent immediately and ammoniacal silver nitrate more slowly. It had $\lambda_{max.}$ 316 mμ (log ε 1·63 in ethanol) and $\nu_{max.}$ (in Nujol) 3478 w, 2645 w, 1744 s, 1720 s, and 1622 w cm.$^{-1}$.

The methyl ester, prepared by means of ethereal diazomethane, had m. p. 151° (Sutter and Schlittler [3] give m. p. 151—152°).

Debromination of β-Bromo-oxopicrotoxinic Acid.—(*a*) To the acid (2 g.) in boiling 95% ethanol (40 ml.) were added ammonium chloride (0·4 g.), in water (2 ml.), and zinc dust (0·6 g.) in small quantities (three such total additions). The volume of solvent was kept constant and reaction restricted to 10—20 min. The excess of zinc was filtered off, the filtrate was reduced to dryness in a vacuum and the residue treated with 2N-sulphuric acid (10 ml.) and kept at 0° for 3 hr., then filtered. The filtrate was continuously extracted with ether. The precipitate was extracted with hot absolute ethanol (4 × 20 ml.), the inorganic residue was rejected, and the combined filtrates were taken to dryness in a vacuum. Crystallisation of the resulting solid from water yielded a mixture (0·95 g.), m. p. 190°. The ether extract yielded further solid (0·06 g.). The combined solids on crystallisation from water yielded the *acid* (VI) in needles, m. p. 219° (Found: C, 59·1; H, 5·6. $C_{15}H_{16}O_7$ requires C, 58·4; H, 5·2%), $\lambda_{max.}$ 340 and 260 mμ (log ε 1·82 and 3·99 respectively in ethanol), $\nu_{max.}$ (in Nujol) 3542, 3397 m, 2730 vw, 2660 vw, 1764 s, 1732 s, 1708 s, 1644 w, 1615 cm.$^{-1}$. The acid did not decolorise bromine water quickly but gave a positive Baeyer's test and reduced Tollens's reagent immediately, but ammoniacal silver nitrate more slowly. Warm alkali gave a deep yellow colour. It did not react with periodic acid.

The *methyl ester*, prepared by treatment with diazomethane and sublimed, had m. p. 171° (Found: C, 60·3; H, 5·75. $C_{16}H_{18}O_7$ requires C, 59·6; H, 5·6%.)

(*b*) Debromination of the acid (2 g.) was carried out as in (*a*) but 5 additions of ammonium chloride–zinc dust were made and the time extended to at least 30 min. On working up after crystallisation from water, an acid crystallising in needles (0·63 g.), m. p. 251°, was obtained. The mother-liquors yielded the acid, m. p. 219° (0·1 g.). Ether extraction of the debromination mother-liquors gave a further yield (0·1 g.) of a mixture of both acids. The *acid*, m. p. 251°, was recrystallised from water for analysis (Found: C, 55·1, 55·0; H, 6·16, 5·9. $C_{15}H_{18}O_8$ requires C, 55·2; H, 5·6%). The acid (V) decolorises bromine-water immediately and gives a positive Baeyer's test. Tollens's reagent is immediately reduced but no colour is obtained by heating the acid with concentrated alkali. Neutral ferric chloride gives a deep yellow colour. The acid reacts with 0·9 and 1·4 equivalents of periodic acid after 2 and 24 hr. respectively.

[8] Jones, Bowers, Halsall, Jones, and Lemin, *J.*, 1953, 2555.

XUM

When the acid was boiled with an excess of sodium hydrogen carbonate solution and then allowed to react with an excess of sodium metaperiodate, the uptake after 22 and 51 hr. amounted to 1·1 and 2·7 equivalents respectively.

Conversion of Acid of M. p. 219° (VI) *into Acid of M. p.* 251° (V).—The acid (VI), m. p. 219° (0·22 g.), was treated with excess of ammonium chloride and zinc dust in a solution of ethanol as described in method (*b*) above. Working up in the same way and crystallisation from water gave an acid, m. p. 251° (0·19 g.), which showed no m. p. depression with the acid (V) obtained as above and possessed identical ultraviolet absorption.

Ozonolysis of Acid (VI).—The acid (VI), m. p. 219°, in ethyl acetate (5 ml.) in an ice–salt bath was treated with ozone–oxygen for 3 hr., by which time the ultraviolet spectrum showed one maximum only, at 285 mμ. The solvent was removed in a vacuum, the resultant glass dissolved in water, and air passed through it into a dilute aqueous solution of 2 : 4-dinitrophenylhydrazine hydrochloride for 1 hr. A yellow precipitate was obtained which after being collected and recrystallised showed no m. p. depression with a sample prepared from acetone. The ozonised product became yellowish-brown when kept, and under a variety of conditions on working up yielded only an intractable gum, $\lambda_{max.}$ 285 mμ.

Periodate Titration.—The acid (VI) (0·5 g.) was ozonised in ethyl acetate until oxidation was complete. The solvent was removed and the ozonide decomposed with water. 0·3M-Periodic acid (10 ml.) was then added and the solution made up to 25 ml. Carbon dioxide was given off for several hours. The amount of periodate consumed amounted to 0·86 and 1·24 equivalents after 2 and 20 hr. respectively. Working up gave intractable oils.

Periodate Oxidation of Acid (V) *of M. p.* 251°.—The acid (V) (0·3 g.) was dissolved in water (40 ml.), 0·3M-periodic acid (6 ml.) was added, and the solution kept for 2 hr. (iodine was liberated after 10 min.), then extracted with ether (4 × 30 ml.) and then continuously for 12 hr. The ether extracts were combined and washed with 10% sodium thiosulphate solution (5 ml.), dried ($MgSO_4$), and evaporated, to yield a straw-coloured gum (0·16 g.). This residue (0·1 g.), in ethanol (5 ml.), was treated with 2 : 4-dinitrophenylhydrazine (0·1 g.) in sulphuric acid (0·5 ml.) and aqueous ethanol (4·5 ml.) and was kept overnight. The orange-red *hydrazone* (0·065 g.) was filtered off and crystallised from ethanol in two forms; orange-yellow, m. p. 255°, and orange-red, m. p. 264° showing no mixed m. p. depression (Found: C, 49·7; H, 4·3; N, 10·0. $C_{21}H_{20}O_{11}N_4$ requires C, 50·0; H, 4·0; N, 11·1%), $\lambda_{max.}$ 363 and 285 mμ (log ε 4·29 and 3·45 respectively), $\lambda_{max.}$ 1775, 1725, 1624, 1595, and 1587 cm.$^{-1}$.

Methyl β-Bromopicrotoxinate and Methylmagnesium Iodide. Product (VII).—Methyl β-bromopicrotoxinate (0·025 mole) was extracted from a Bolton extractor into refluxing ethereal methylmagnesium iodide (0·2 mole). Refluxing was continued for 1 hr. after extraction, and the complex then hydrolysed with ice (50 g.) and excess of 4N-sulphuric acid. Sodium hydrogen carbonate was added until the solution was neutral to litmus, the ether layer separated, and the aqueous phase extracted with ether (4 × 50 ml.) and then ethyl acetate (5 × 100 ml.). The combined extracts were dried (Na_2CO_3) and the solvent was removed to give a brown solid (85% yield) which crystallised from chloroform, ethanol, water, or, preferably, ethyl acetate, to give the *alcohol* (VII), prisms, m. p. 227° (Found: C, 50·7, 51·0, 51·2; H, 6·0, 6·4, 5·5; Br, 18·8. $C_{19}H_{27}O_6Br$ requires C, 51·5; H, 6·5; Br, 19·1%), $\lambda_{max.}$ 222 mμ (log ε 2·44), $\nu_{max.}$ (in Nujol) 3543 and 3227 m cm.$^{-1}$, giving negative unsaturation and reducing tests.

The alcohol (VII) (0·1 g.) was kept in pyridine (1 ml.)–acetic anhydride (2 ml.) at room temperature for 24 hr. Addition of water and removal of solvent afforded a gum which on repeated distillation (160°/0·01 mm.) gave a *monoacetate* as a colourless glass, m. p. 82° (Found: C, 51·6; H, 6·2; Br, 17·3. $C_{20}H_{29}O_7Br$ requires C, 52·05; H, 6·3; Br, 17·3%), stable to chromic acid in acetone, $\lambda_{max.}$ 220 mμ (log ε 2·42), $\nu_{max.}$ 3438, 1740 m, and 1700 (infl.) cm.$^{-1}$.

Where the Grignard complex was decomposed by a saturated solution of ammonium chloride, a brown gum was obtained from which, by counter-current distribution between water and ethyl acetate–ether (1 : 1), the alcohol (VII), m. p. 227°, was obtained as the major product and in a minor yield a *ketone*, m. p. 241° (needles from ethanol) (Found: C, 51·2; H, 5·7; Br, 20·2. $C_{17}H_{23}O_6Br$ requires C, 50·6; H, 5·7; Br, 19·8%), $\lambda_{max.}$ 220 and 290 mμ, $\nu_{max.}$ (in Nujol) 3462 s, 2650, 2320, and 1699 s cm.$^{-1}$.

Periodate Oxidation of the Alcohol (VII).—The alcohol (0·98 g.) was stirred in 0·5N-periodic acid (20 ml.) for 24 hr. at 20°. Air was bubled through the solution and passed into a saturated solution of 2 : 4-dinitrophenylhydrazine in N-sulphuric acid. The precipitated acetone dinitrophenylhydrazone (65% yield) had m. p. and mixed m. p. 125°. The reaction solution was

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extracted with ether (5 × 100 ml.), then ethyl acetate (4 × 100 ml.), and the combined extracts were distilled into a 2 : 4-dinitrophenylhydrazine solution to give a further 16% of acetone derivative. The residual *ketone* (VIII; R = Me, R′ = :O) (0·85 g.) crystallised as needles (from ethyl acetate), m. p. 223° (Found: C, 50·2; H, 5·2. $C_{15}H_{19}O_5Br$ requires C, 50·1; H, 5·3%), $\lambda_{max.}$ 223 and 301 mμ (log ε 2·36 and 1·52 respectively), $\nu_{max.}$ 3488 m and 1767 cm.$^{-1}$.

In a quantitative periodate oxidation the excess of periodic acid was determined in the usual manner by back-titration; 1·01 equivs. were consumed after 2·3 hr. and 1·19 equivs. after 24 hr. Oxidation with sodium periodate or lead tetra-acetate of the alcohol (VII) yielded the ketone, m. p. 223°, described above. The ketone was recovered after treatment with selenium dioxide, or with ethanolic benzaldehyde and sodium ethoxide. It was stable towards 0·2N-sulphuric acid at 100° but gave an intractable brown gum with 2N-acid at 100°. The *acetate*, prepared by reaction with acetic anhydride–pyridine and crystallised from water, had m. p. 144° (Found: C, 51·4; H, 5·0. $C_{17}H_{21}O_6Br$ requires C, 50·9; H, 5·3%), $\lambda_{max.}$ 223 and 300 mμ (log ε 2·32 and 1·48 respectively), $\nu_{max.}$ 1762 s and 1729 cm.$^{-1}$. The acetate (0·01 g.) and 2N-periodic acid (2 ml.) were kept for 15 hr. at room temperature; water (10 ml.) was added and the mixture was shaken with ether; the ether layer was distilled into a solution of 2 : 4-dinitrophenylhydrazine; this solution was then extracted with light petroleum (5 × 100 ml.) and the residue run on a chromatogram to give R_F 0·90 identical with that of acetone 2 : 4-dinitrophenylhydrazone under the same conditions (ether–light petroleum 1 : 19).

Chromic Acid Oxidation of the Ketone (VIII; R = Me, R′ = :O).—The ketone obtained as above (0·05 g.), in acetone (2 ml.), was mixed with chromic anhydride (0·02 g.) and 4N-sulphuric acid (1 ml.). After 24 hr. sodium sulphite solution in excess was added, and the solution extracted with ether. Evaporation of the extract gave a *diketone* (0·03 g.) which, recrystallised from aqueous ethanol, had m. p. 191° (Found: C, 50·25; H, 5·0; Br, 22·5. $C_{15}H_{17}O_5Br$ requires C, 50·4; H, 4·8; Br, 22·4%), $\lambda_{max.}$ 316 mμ (log ε 1·89), $\nu_{max.}$ 1769 m and 1749 m cm.$^{-1}$, stable to further periodic and chromic acid oxidation. The 2 : 4-*dinitrophenylhydrazone* crystallised as needles (from chloroform–ethanol), m. p. 267° (Found: C, 46·0; H, 3·4; Br, 14·9, 15·0; N, 10·1. $C_{21}H_{21}O_8N_4Br$ requires C, 46·9; H, 3·9; Br, 14·9; N, 10·4%).

Chromic Acid Oxidation of Alcohol (VII).—The alcohol (0·97 g.) in acetone (10 ml.) was kept overnight with chromic anhydride (0·5 g.) and 4N-sulphuric acid (5 ml.). An excess of sodium sulphite, in water (50 ml.), was added, and the aqueous solution extracted with ether. The extract was dried (Na_2SO_4), and evaporated. The residue, in ethanol, was passed down an alumina column and crystallised from ethanol–water, to yield the above diketone (0·42 g.), m. p. 191°. From the mother-liquors two further *ketones* were isolated. The first (0·09 g.), obtained by repeated recrystallisation from aqueous ethanol, had m. p. 209° (Found: C, 48·5; H, 5·1; Br, 18·8. $C_{17}H_{21}O_7Br$ requires C, 48·9; H, 5·1; Br, 19·15. $C_{17}H_{23}O_7Br$ requires C, 48·7; H, 5·5; Br, 19·16%), $\lambda_{max.}$ 315 mμ (log ε 1·36), $\nu_{max.}$ 3608, 3518, 3408, 3318, and 1741 s cm.$^{-1}$, giving no iodoform reaction. The second ketone was obtained by repeated sublimation (150°/0·02 mm.) (about 10% yield) and had m. p. 230° (Found: C, 51·4; H, 5·7; Br, 19·7. $C_{16}H_{25}O_6Br$ requires C, 51·8; 6·0; Br, 19·15%), $\lambda_{max.}$ 299 mμ (log ε 1·72), $\nu_{max.}$ 3363 m, 1755 s, and 1701 s cm.$^{-1}$.

Debromination of Ketone (VIII; R = H, R′ = OH).—The ketone (0·5 g.), in water (10 ml.), was debrominated in the usual manner for 10 min. by zinc (0·3 g.) and ammonium chloride (0·3 g.). The colourless solution was filtered, acidified with 2N-sulphuric acid, and continuously extracted with ether. The debrominated *product* (0·2 g.) was purified by sublimation at 150°/0·02 mm. and crystallisation from water to m. p. 215—218° (Found: C, 63·4; H, 6·7. $C_{14}H_{18}O_5$ requires C, 63·1; H, 6·8%). The compound did not reduce ammoniacal silver nitrate, but decolorised bromine water and after 24 hr. at 18° with periodic acid had consumed 0·45 mole. It had $\lambda_{max.}$ 301 mμ (log ε 1·47) and $\nu_{max.}$ 3426 s and 1753 s cm.$^{-1}$.

β-*Bromopicrotoxinic Acid and Methylmagnesium Iodide*.—The acid (2·12 g. 0·005 mole) was extracted from a thimble into ethereal methylmagnesium iodide (0·05 mole). Refluxing was continued for a further hour after extraction, the mixture was cooled and hydrolysed with N-sulphuric acid (100 ml.), and the ether layer decanted. The aqueous layer was extracted first with ether (3 × 100 ml.) and then with ethyl acetate (3 × 100 ml.), and the combined extracts were reduced to dryness, yielding much iodine and an *acid* (0·05 g.), crystallising as needles, m. p. 215°, from water (Found: C, 47·05; H, 4·4. $C_{16}H_{21}O_7Br$ requires C, 47·4; H, 5·2%). The acid did not react with periodic acid.

Lead Tetra-acetate Oxidation.—The above acid (0·02 g.) and lead tetra-acetate (0·05 g.) were

warmed together in glacial acetic acid (2 ml.) at 50° for 1 hr., then kept at room temperature overnight. Addition of water (30 ml.) and ether-extraction gave a yellow oil which on sublimation at 130°/0·02 mm. gave the ketone (VIII; R = Me, R′ = :O) (0·01 g.), m. p. and mixed m. p. 218°.

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27. *Stereochemical Investigations of Cyclic Bases. Part IV.* Hofmann Degradation of 6α- and 6β-Cholestanyltrimethylammonium Salts.*

By B. B. GENT and J. MCKENNA.

Cholestan-6-one has been obtained as a by-product of formaldehyde–formic acid methylation of 6β-aminocholestane but not of the 6α-epimer; and 6β-cholestanyltrimethylammonium salts are much less stable that the 6α-analogues. These effects probably arise from steric interaction of the 6β-(axial)-nitrogenous group with the angular 10-methyl group; the reaction of cholestan-6α-yl toluene-*p*-sulphonate with dimethylamine, however, is accompanied by Walden inversion. Nearly pure cholest-5-ene was obtained by Hofmann fission of 6β-cholestanyltrimethylammonium salts even under strongly alkaline conditions, while pyrolysis of 6α-cholestanyltrimethylammonium hydroxide resulted mainly in reversion to the tertiary steroid base, but yielded also a little cholest-5- and -6-ene.

PREVIOUS examination [1] of the Hofmann degradation of a number of steroidal trimethylammonium salts with the quaternary group attached to $C_{(3)}$ has shown that axial salts are readily degraded to olefins while the equatorial epimers preferentially revert to tertiary steroid bases. The degradation of epimeric 6-cholestanyltrimethylammonium salts described in this paper follows the same pattern, but the results include additional features of mechanistic and stereochemical interest.

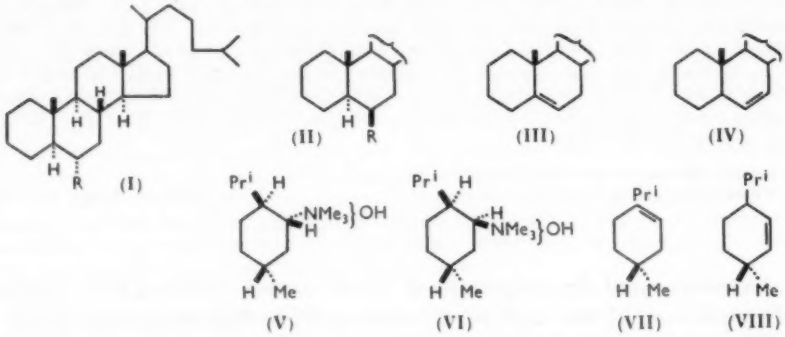
6α-Aminocholestane (I; R = NH_2) was prepared by reduction of the oxime of either cholestan-6-one or 3β-chlorocholestan-6-one with sodium and ethanol or pentanol; a little of the 6β-amine (II; R = NH_2) was also obtained from one of these reactions, and this base was in our hands the sole product of reduction of cholestan-6-one oxime or 6-nitrocholest-5-ene with lithium aluminium hydride. Our use of a large excess of hydride in the ketoxime reduction appears to have suppressed the formation of a little 6α-amine which has been reported by other workers.[2,3] The configurations of the primary bases are evident from the methods of preparation and from other work previously reported,[2,3] and are supported by the degradations described in this paper.

Methylation of 6β-aminocholestane with formaldehyde and formic acid yielded the tertiary base (II; R = NMe_2) together with cholestan-6-one; an identical tertiary base

* Part III, *J.*, 1958, 2759.

[1] Haworth, McKenna, and Powell, *J.*, 1953, 1110; Gent and McKenna, *J.*, 1956, 573.
[2] Shoppee, Evans, and Summers, *J.*, 1957, 97.
[3] Bird and Cookson, *Chem. and Ind.*, 1955, 1479.

was obtained by methylation with methyl iodide and potassium carbonate, so that no appreciable racemisation occurred during the first reaction in spite of the possibility of equilibrium of intermediates $>CH\cdot N{:}CH_2 \rightleftharpoons >C{:}N\cdot CH_3$ suggested by ketone formation. This accords with previous experience.[4,5] 6β-Cholestanyltrimethylammonium iodide (II; R = NMe_3}I) was very unstable, and readily yielded cholest-5-ene (III) and trimethylammonium iodide on being heated either alone or in organic solvents. Care was



therefore necessary to avoid extensive decomposition of the methiodide during methylation, particularly as the quaternisation was rather slow; further, it was necessary to use alkali (potassium carbonate) even in the direct conversion of the *tertiary* base into the methiodide in order to prevent formation of the base hydriodide [6] (together with cholest-5-ene and tetramethylammonium iodide). All samples of cholest-5-ene obtained by degradation of 6β-cholestanyltrimethylammonium iodide were of quite high purity, and, in particular, no evidence for admixture with cholest-6-ene was obtained. The same was true for the hydrocarbon obtained from the quaternary hydroxide (II; R = NMe_3}OH) by either rapid heating or vacuum-concentration of its methanolic solution at room temperature.

No cholestan-6-one was isolated after methylation of 6α-aminocholestane with formaldehyde and formic acid, and the related quaternary salt (I; R = NMe_3}I) was stable in low-boiling organic solvents but lost methyl iodide on fusion. Pyrolysis of the quaternary hydroxide (I; R = NMe_3}OH) gave 6α-dimethylaminocholestane (I; R = NMe_2) and a low yield of neutral product which was cholest-6-ene (IV) mixed with a considerable proportion of cholest-5-ene (III).

We believe that the formation of cholestan-6-one during formaldehyde–formic acid methylation of 6β- but not 6α-aminocholestane is related to the considerable steric interaction between the axial 10-methyl group and the axial basic centre. The same stereochemical feature appears to be responsible for the instability of the 6β-cholestanyltrimethylammonium salts, which in this respect resemble in their properties the metho-salts of Mannich bases. Shoppee and Howden [7] have shown that reaction of cholestan-6α-ol with phosphorus pentachloride or pentabromide yields the 6α-halides, but we have found that the 10-methyl group does not prevent Walden inversion in the reaction of cholestan-6α-yl toluene-*p*-sulphonate with the strong nucleophile dimethylamine (although extensive elimination yielding cholest-5-ene also occurs). There is an interesting analogy between these results and those of substitution at $C_{(3)}$ in 5 : 6-unsaturated steroids.[8,9]

[4] Parham, Hunter, Hanson, and Lahr, *J. Amer. Chem. Soc.*, 1953, **75**, 5646; Grob, Kny, and Gagneux, *Helv. Chim. Acta*, 1957, **40**, 130.
[5] McKenna and Slinger, *J.*, 1958, 2759.
[6] Cf. Rapoport, Campion, and Gordon, *J. Amer. Chem. Soc.*, 1955, **77**, 2389.
[7] Shoppee and Howden, *Chem. and Ind.*, 1958, 414.
[8] Pierce, Richards, Shoppee, Stephenson, and Summers, *J.*, 1955, 694.
[9] Haworth, Lunts, and McKenna, *J.*, 1955, 986.

The direction of elimination in the Hofmann degradations reported is of some interest in that (*a*) formation of a considerable proportion of cholest-5-ene by fission of 6α-cholestanyltrimethylammonium hydroxide (5α-H) is obviously not a *trans*-elimination (relevant factors may be the rigidity of ring B and the equatorial disposition of the 6α-quaternary group) and (*b*) the apparently exclusive formation of cholest-5-ene from 6β-cholestanyltrimethylammonium salts does not correspond to anion-attack on hydrogen attached to the least alkylated β-carbon atom, which is $C_{(7)}$ (and carries a suitably oriented axial hydrogen atom). The results parallel those obtained with menthyl- (V) * and *neo*menthyl-trimethylammonium hydroxide (VI) which have been investigated and discussed by several groups of workers; [10] in particular, H. C. Brown and his collaborators regard the preponderant fission of the hydroxide (VI) to menth-3-ene (VII) rather than to menth-2-ene (VIII) as supporting their theory of the directive forces in bimolecular Hofmann eliminations. We have made no detailed kinetic study of any of the eliminations reported in this paper, but conditions in the formation of cholest-5-ene, at least from fused 6β-cholestanyltrimethylammonium hydroxide, would be expected to favour strongly a bimolecular elimination,[5] and the rate of fission of the 6β-quaternary iodide in boiling ethanol has been qualitatively shown to be sensitive to added alkali.

Experimental

Optical rotations refer to chloroform solutions at room temperature (17—23°) at concentrations (except where otherwise stated) of 1—3%. Light petroleum refers to the fraction of b. p. 40—60°.

6α- *and* 6β-*Aminocholestane.*—(*a*) Cholestan-6-one oxime (0·65 g.) in boiling pentanol (60 c.c.) was saturated with sodium during 1·5 hr. and the organic reduction products were treated with hydrochloric acid, yielding a mixture of 6α- (0·43 g.) and 6β-aminocholestane hydrochloride (0·18 g.), which were readily separated by utilising the remarkable fact that the 6β-hydrochloride is freely soluble, not only in ether (as in the 3 : 5-*cyclo*-analogue),[1, 9, 11] but also in light petroleum. After crystallisation from alcohol **6α-*aminocholestane hydrochloride*** was obtained as rectangular prisms, m. p. 300°, $[\alpha]_D$ +34° (Found: C, 76·0; H, 12·0; N, 2·9. $C_{27}H_{50}NCl$ requires C, 76·5; H, 11·9; N, 3·3%), insoluble in water, ether, and light petroleum. 6α-Aminocholestane separated from methanol in prisms, m. p. 127—129°, $[\alpha]_D$ +38° (Found: C, 83·3; H, 12·7; N, 3·4. Calc. for $C_{27}H_{49}N$: C, 83·7; H, 12·7; N, 3·6%). The 6β-hydrochloride was recrystallised from acetone–ether and then converted into the amine, m. p. 108° undepressed on admixture with 6β-aminocholestane prepared by method (*b*).

6α-Aminocholestane was also obtained by reduction of 3β-chlorocholestan-6-one oxime as described above, and ethanol has been substituted for pentanol in each case; these earlier experiments, however, were carried out before we had noted the unusual solubility of 6β-aminocholestane hydrochloride in light petroleum, and this isomer was not therefore identified in reaction mixtures where it was probably present in small quantities.

(*b*) 6-Nitrocholest-5-ene (3 g.) in boiling ether (80 c.c.) was reduced with lithium aluminium hydride (1·5 g.) for 4 hr. and the resulting base (2·5 g.) converted into the hydrochloride, which was completely soluble in light petroleum. After recrystallisation of the salt from acetone–ether, the **6β-*aminocholestane hydrochloride*** formed prisms, m. p. 190—192°, optically almost inactive ($[\alpha]_D$ *ca.* −1°; *c* 10%) (Found: C, 76·7; H, 11·6; N, 2·9; Cl, 8·5%. $C_{27}H_{50}NCl$ requires C, 76·5; H, 11·9; N, 3·3; Cl, 8·4%). 6β-Aminocholestane, prepared from the purified hydrochloride and recrystallised from ethanol, had m. p. 108°, $[\alpha]_D$ +11° (Found: C, 83·6; H, 12·7%).

(*c*) Reduction of cholestan-6-one oxime (1·1 g.) in boiling ether (100 c.c.) with lithium aluminium hydride (3 g.) for 48 hr. and purification of the basic product (1 g.) as described above

* Formulæ (V—VIII) represent the quaternary hydroxides derived from (−)-menthylamine and (+)-*neo*menthylamine used in the investigations, and the isomeric derived (+)-menthenes.

[10] Brown and Moritani, *J. Amer. Chem. Soc.*, 1956, **78**, 2203; Cope and Acton, *ibid.*, 1958, **80**, 355; these authors give references to earlier work.

[11] Julian, Magnani, Meyer, and Cole, *ibid.*, 1948, **70**, 1834.

gave 6β-aminocholestane, m. p. 108° (undepressed with the compound derived from 6-nitrocholest-5-ene), $[\alpha]_D$ +13°.

The physical properties observed for 6α-aminocholestane agree with those given by other authors,[2, 12] but Shoppee, Evans, and Summers [2] have recorded m. p. 94—96°, $[\alpha]_D$ +6·3°, for 6β-aminocholestane.

Methylation of 6β-*Aminocholestane.*—(*a*) 6β-Aminocholestane (0·9 g.) was heated on a steam-bath with 40% aqueous formaldehyde (1·5 c.c.), 98% formic acid (1·5 c.c.), and water (3 c.c.) for 4 hr. After evaporation with excess of hydrochloric acid the products were separated with ether into 6β-dimethylaminocholestane hydrochloride (0·8 g.) and cholestan-6-one (0·1 g.). The latter was recrystallised from alcohol and identified by its m. p. and mixed m. p. (96°), infrared spectrum, and conversion into the oxime, m. p. and mixed m. p. 195°. 6β-*Dimethylaminocholestane hydrochloride* separated from acetone–chloroform in regular rectangular prisms, m. p. 255—257°, $[\alpha]_D$ +15° (Found: C, 76·6; H, 11·8; N, 3·2; Cl, 7·6. $C_{29}H_{54}NCl$ requires C, 77·0; H, 12·0; N, 3·1; Cl, 7·8%), soluble in water but not in dilute hydrochloric acid, ether, or light petroleum. 6β-*Dimethylaminocholestane*, obtained from the recrystallised hydrochloride, was an oil (resembling in this respect the 3 : 5-*cyclo*-analogue [5, 13]), b. p. 170° (bath)/0·005 mm., $[\alpha]_D$ −8° (Found: C, 83·6; H, 13·0. $C_{29}H_{53}N$ requires C, 83·9; H, 12·8%).

(*b*) A solution of 6β-aminocholestane (0·9 g.) in methyl iodide (8 c.c.) and methyl alcohol (3 c.c.) was refluxed gently with powdered anhydrous potassium carbonate (2 g.) for 6 hr., the mixture was evaporated to dryness under reduced pressure, and the residue extracted with cold chloroform (which does not dissolve tetramethylammonium iodide; cf. results described in the following paragraph). The extract was evaporated at *room temperature* under reduced pressure and the residue was separated with light petroleum into soluble (0·5 g.) and insoluble (0·5 g.) fractions. The former was treated with hydrochloric acid and the resulting mixture separated into 6β-dimethylaminocholestane hydrochloride (0·4 g.) which after recrystallisation from acetone–chloroform was identical in m. p. and infrared spectrum with the product prepared as in the preceding paragraph, and cholest-5-ene (0·1 g.), m. p. and mixed m. p. 91—92° after recrystallisation from ethanol. The petroleum-insoluble product was 6β-*cholestanyltrimethylammonium iodide*, which had m. p. 120—140° (rapid heating) after drying at 20°/0·005 mm.; the melting range (which was lowered on storage) appears to be due to partial Hofmann fission, and the ready similar degradation in hot organic solvents (see following paragraphs) discouraged attempts at recrystallisation, but the freshly prepared salt appeared to be pure (Found: N, 2·7; I, 22·5. $C_{30}H_{56}NI$ requires N, 2·5; I, 22·8%).

Hofmann Fission of 6β-*Cholestanyltrimethylammonium Salts.*—(*a*) The ready degradation of 6β-cholestanyltrimethylammonium iodide was first encountered during attempts to prepare the salt from the tertiary base in the usual manner. For example, the tertiary base (0·5 g.) was refluxed overnight with acetone (10 c.c.) and methyl iodide (5 c.c.), the solution was evaporated, and the residue was separated with light petroleum into soluble (0·20 g.) and insoluble (0·39 g.) fractions. The former was identified as cholest-5-ene by m. p. (90—91° before recrystallisation, 92° after recrystallisation from alcohol), mixed m. p., infrared spectrum, and specific rotation ($[\alpha]_D$ of unpurified product, −52°). The petroleum-insoluble solid was separated with boiling acetone into soluble (0·3 g.) and insoluble (90 mg.) fractions, and the latter, m. p. >360° after recrystallisation from aqueous acetone, was identified as tetramethylammonium iodide (Found: I, 62·8. Calc. for $C_4H_{12}NI$: I, 63·2%) by its infrared spectrum. The acetone-soluble compound after recrystallisation from the same solvent formed regular rectangular prisms, m. p. 258—260°, and was identified as 6β-*dimethylaminocholestane hydriodide* * by conversion into the oily tertiary base and formation therefrom in the usual manner, infrared comparison with an authentic specimen, and analysis (Found: C, 64·0; H, 9·9; I, 22·9. $C_{29}H_{54}NI$ requires C, 64·1; H, 9·9; I, 23·4%).

(*b*) 6β-Cholestanyltrimethylammonium iodide (150 mg.) in chloroform (2 c.c.) was refluxed for 3 hr.: a heavy precipitate began to appear during the first few minutes' heating. The solvent was evaporated and the residue was extracted with ether which removed cholest-5-ene

* These results prompted re-examination of the salt obtained [5] together with cholesteryl iodide and tetramethylammonium iodide from 6β-dimethylamino-3 : 5-*cyclo*cholestane by treatment with methyl iodide in acetone, and previously described as the methiodide. This salt is also in fact a hydriodide. The chemistry of 3 : 5-*cyclo*-bases will be discussed further in a later communication.

[12] Vanghelovici and Vasiliu, *Bull. Soc. chim. România*, 1935, **17**, 249 (*Chem. Abs.*, 1936, **30**, 7119).
[13] Šorm, Lábler, and Černý, *Chem. Listy*, 1953, **47**, 418.

(90 mg.); the residue was then washed with chloroform, and the insoluble product (50 mg.) was recrystallised from acetone. It had m. p. 230—240° (Found: I, 67·8. Calc. for $C_9H_{16}NI$: I, 67·9%) and its infrared spectrum was identical with that of authentic trimethylammonium iodide.

(*c*) Quaternary iodide (0·12 g.) in methanol (10 c.c.) and water (2 c.c.) was shaken for 8 hr. with excess of silver oxide, silver salts were filtered off, and the filtrate was evaporated overnight in a vacuum-desiccator (solid KOH). When the desiccator was opened a strong odour of volatile amine was noted; the waxy residue was therefore washed with ether which removed cholest-5-ene (50 mg.), m. p. and mixed m. p. 88—89° before, 91—92° after, recrystallisation from ethanol, $[\alpha]_D$ −55° (purified sample). Infrared spectroscopic examination of the crude sample gave no indication of the presence of cholest-6-ene. The ether-insoluble residue fused with evolution of volatile base when heated rapidly to 100—140°; ether then extracted more cholest-5-ene (5 mg.), m. p. and mixed m. p. 88—89° before, 91—92° after, recrystallisation from ethanol.

(*d*) The quaternary iodide was cleaved nearly quantitatively into cholest-5-ene and trimethylammonium iodide by being heated for 4 min. at 170°.

Effect of Base on Rate of Hofmann Fission of 6β-Cholestanyltrimethylammonium Iodide in Ethanol.—The following is typical of several groups of experiments. The same reflux apparatus was used throughout, and boiling was always attained by immersion in a boiling water-bath to just above the level of the methiodide solution.

(*a*) A solution of the methiodide (20 mg.) in 0·5N-ethanolic potassium hydroxide (1 c.c.) was refluxed for 10 min. and cooled to 15°; crystals (cholest-5-ene) were deposited. The mixture was diluted with light petroleum (4 c.c.), water (4 c.c.) was added, and after shaking and separation of the phases the aqueous-alcohol layer was extracted three times further with light petroleum (4 c.c.). The total petroleum extract yielded cholest-5-ene (13 mg.; theoretical).

(*b*) A solution of the methiodide (20 mg.) in ethanol (1 c.c.) deposited no significant quantity of crystals when refluxed even for 20 min., cooled to 15°, and seeded with cholest-5-ene. Application of the extraction technique described in the preceding paragraph, however, yielded cholest-5-ene (5 mg.). Undecomposed methiodide (12 mg.) was then extracted by chloroform from its suspension in the aqueous-alcohol layer.

(*c*) A solution of the methiodide (20 mg.) in ethanol (1 c.c.) gave a quantitative yield of cholest-5-ene after being refluxed for 2 hr.

Methylation of 6α-Aminocholestane.—Methylation of the primary amine with formaldehyde and formic acid gave *6α-dimethylaminocholestane*, which separated from acetone in prisms, m. p. 64—65°, $[\alpha]_D$ +50° (Found: C, 84·2; H, 13·0; N, 3·3. $C_{29}H_{53}N$ requires C, 83·9; H, 12·8; N, 3·4%); the tertiary base was best purified *via* the *hydrochloride*, irregular leaflets (from chloroform–ether), m. p. 260—265°, $[\alpha]_D$ +41° (Found: C, 77·1; H, 12·3. $C_{29}H_{54}NCl$ requires C, 77·0; H, 12·0%). This salt was soluble in water but not in dilute hydrochloric acid, ether, or light petroleum. When the tertiary base was refluxed in acetone with methyl iodide, or when the primary base was refluxed in methanol with methyl iodide and potassium carbonate, the only organic product was *6α-cholestanyltrimethylammonium iodide*, m. p. 140—200° (Found: N, 2·5; I, 22·9. $C_{30}H_{56}NI$ requires N, 2·5; I, 22·8%); the m. p. range was not reduced on recrystallisation and appears to be due to partial decomposition during heating (see next paragraph).

Hofmann Fission of 6α-Cholestanyltrimethylammonium Salts.—(*a*) The quaternary iodide (60 mg.) was heated at 200—210° for 4 min., and the mixture was then cooled and extracted with ether. The extract contained a neutral oil (6 mg.) and 6α-dimethylaminocholestane (29 mg.), m. p. and mixed m. p. 62—64° after recrystallisation from acetone.

(*b*) The methiodide (0·3 g.) was converted in the usual manner into the quaternary hydroxide which was decomposed at 175—195°/0·02 mm. Extraction with ether gave 6α-dimethylaminocholestane (175 mg.), m. p. (from acetone) 62—64°, and a neutral fraction (15 mg.) which were separated by hydrochloric acid treatment. The neutral fraction had m. p. 55—65° (raised to 70—72° by recrystallisation from methanol) and $[\alpha]_D$ −67° (the specific rotations of cholest-5-ene and cholest-6-ene have recently been given [14] as −55° and −84° respectively. The strongest band in the C–H deformation area was at 770 cm.$^{-1}$, and this is attributed to cholest-6-ene,[15] but bands at 797 and 836 cm.$^{-1}$ due to cholest-5-ene [16] were also prominent. Reduction

[14] Turner, Meador, and Winkler, *J. Amer. Chem. Soc.*, 1957, **79**, 4122.
[15] Henbest, Meakins, and Wood, *J.*, 1954, 800.
[16] Bladon, Fabian, Henbest, Koch, and Wood, *J.*, 1951, 2402.

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of the mixture with hydrogen and platinium in acetic acid–ether gave cholestane which was pure after a single recrystallisation from methanol, having m. p. and mixed m. p. 79—80°.

Reaction of Cholestan-6α-yl Toluene-p-sulphonate with Dimethylamine.—The ester,[17] m. p. 108° (109 mg.), was heated in a steel autoclave with an excess of dimethylamine at 120° for 4 days, the mixture was treated with excess of aqueous sodium hydroxide and extacted with ether, and the ether was evaporated. Treatment of the residue with hydrochloric acid gave the ether-insoluble 6β-dimethylaminocholestane hydrochloride (18 mg.) which after recrystallisation from carbon tetrachloride–chloroform had m. p. 258—260°, $[\alpha]_D$ +13° (Found: C, 77·3; H, 11·9. Calc. for $C_{29}H_{54}NCl$: C, 77·0; H, 12·0%). The infrared spectrum of this salt was identical with that of samples prepared from 6β-aminocholestane, and likewise the derived tertiary base was degraded to cholest-5-ene on attempted quaternisation with methyl iodide in boiling acetone.

The neutral product from the autoclave experiment was crude cholest-5-ene, which had m. p. and mixed m. p. 88—89° after purification by chromatography on alumina; when the reaction was run at 100° for 16 hr., however, some of the ester was also recovered, and the yield of tertiary base was correspondingly reduced.

The authors thank the Department of Scientific and Industrial Research for a Maintenance Grant (to B. B. G.), and Mr. A. Tulley for a preparation of 6α-aminocholestane.

THE UNIVERSITY, SHEFFIELD. [*Received, August 28th*, 1958.]

[17] Karrer, Asmis, Sareen, and Schwyzer, *Helv. Chim. Acta*, 1951, **34**, 1022; Shoppee and Summers, *J.*, 1952, 1786.

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28. *The Electronic Interaction between Benzenoid Rings in Condensed Aromatic Hydrocarbons.* 1 : 12-2 : 3-4 : 5-6 : 7-8 : 9-10 : 11-*Hexabenzocoronene*, 1 : 2-3 : 4-5 : 6-10 : 11-*Tetrabenzoanthanthrene*, *and* 4 : 5-6 : 7-11 : 12-13 : 14-*Tetrabenzoperopyrene.*

By E. CLAR, C. T. IRONSIDE, and M. ZANDER.

Hexabenzocoronene was synthesised from 2 : 3-7 : 8-dibenzoperinaphthene. The unstable perbromide of the dibenzoperinaphthene decomposed when melted and condensed to tetrabenzoperopyrene which was cyclised to hexabenzocoronene. Phenyltribenzoperylene, obtained from dibenzoperylene and phenylacetylene, was cyclised to tetrabenzanthanthrene in a sodium chloride–aluminium chloride melt.

Comparison of the absorption spectra of benzene, triphenylene, 1 : 2-6 : 7-dibenzopyrene, 1 : 12-2 : 3-10 : 11-tribenzoperylene, tetrabenzanthanthrene (VI) and hexabenzocoronene (III) shows the varying degree of electronic interaction between the benzenoid rings * of these hydrocarbons, attributed mainly to contact bonds.

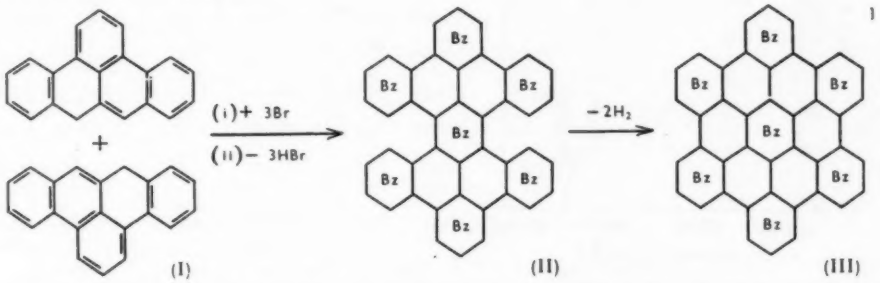
RECENTLY [1] it was shown that the aromatic hydrocarbons triphenylene, dibenzopyrene, tetrabenzanthracene, and tribenzoperylene, containing exclusively benzenoid rings * interlinked by quasi-single bonds, have a very low reactivity. They do not dissolve in concentrated sulphuric acid and show strong phosphorescence of very long life at low temperature. Their absorption bands are shifted more to the violet than are those of the isomeric aromatic hydrocarbons, except for the corresponding polyphenyls with the same number of benzenoid rings; their chemical inertness may be related to this fact.

* In view of the discussion in this paper and to avoid the implication of a particular Kekulé structure, double bonds are omitted from the formulæ unless the discussion requires their inclusion. Bz is used to indicate a ring having benzenoid character, in the sense discussed here and in *J.*, 1958, 1863. No other significance is implied.

[1] Clar and Zander, *J.*, 1958, 1861.

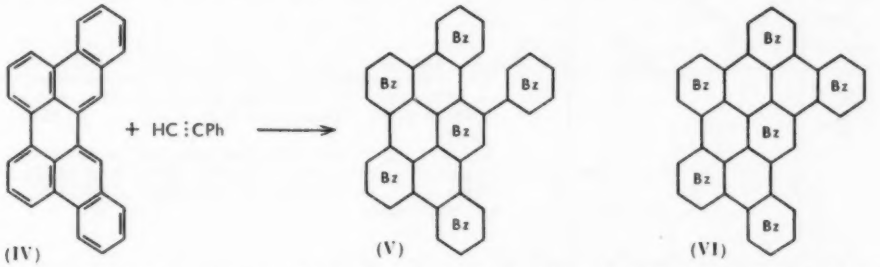
We have now synthesised another hydrocarbon of this kind, hexabenzocoronene (III), which in addition to these properties has a high degree of symmetry.

2 : 3-7 : 8-Dibenzoperinaphthene (I) [2] in benzene with bromine gave a deep brown perbromide, $C_{21}H_{14}Br_3$, from which the hydrocarbon could be recovered on dissolution in acetone. However, in boiling trichlorobenzene, or when melted, the perbromide gave three molecules of hydrogen bromide and the orange tetrabenzoperopyrene (II). The microwave absorption method showed that the perbromide was not paramagnetic.[3] A similar compound, the adduct of one atom of bromine and one molecule of benzanthrone,[4] also was not paramagnetic.[3] This can be explained if the perbromide formed reversibly a crystalline dimer or polymer.



(I) (II) (III)

Tetrabenzoperopyrene (II) melted in an evacuated capillary at 482° with evolution of hydrogen, then resolidified and did not melt again below 700°. The extreme stability of hexabenzocoronene, which can be readily sublimed or crystallised from boiling pyrene at about 390°, can be related to formula (III) which contains exclusively benzenoid rings interlinked by quasi-single bonds. This pale yellow hydrocarbon did not dissolve in cold concentrated sulphuric acid and showed an orange-yellow phosphorescence of very long life in solid solution in trichlorobenzene at low temperature, both properties being typical of this kind of hydrocarbon. Hexabenzocoronene (III) can also be obtained by melting dibenzoperinaphthene (I) with sulphur or by sublimation of the distillation residue from the preparation of dibenzoperinaphthene.[2]



(IV) (V) (VI)

The absorption spectrum of hexabenzocoronene is given in Fig. 1 and that of tetrabenzoperopyrene (II) in Fig. 2. The latter is closely related to that of 4 : 5-11 : 12-dibenzoperopyrene; [5] however, twisting of the molecular plane caused by the four overlapping hydrogen atoms produces a broadening of the *p*-bands. In order to complete the series of hydrocarbons with 1, 2, 3, 4, 5, and 7 benzenoid rings [see (VII)] the missing member with 6 benzenoid rings, 1 : 2-3 : 4-5 : 6-10 : 11-tetrabenzoanthanthrene (VI) was

[2] Clar, *Ber.*, 1943, **76**, 611.
[3] This investigation was kindly carried out by Mr. P. Carmichael, Department of Natural Philosophy.
[4] Brass and Clar, *Ber.*, 1936, **69**, 690; Müller and Wiesemann, *Ber.*, 1936, **69**, 2173; Schwab and Schwab-Agallidis, *Z. phys. Chem.*, *B*, 1941, **49**, 196.
[5] Clar, *Ber.*, 1943, **76**, 458.

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synthesised from the dibenzoperylene (IV).[1] The dibenzoperylene with phenylacetylene formed the phenyltribenzoperylene (V), involving similar intermediate stages to those reported in the analogous reaction with maleic anhydride.[1] The spectrum of the hydro-

FIG. 1.

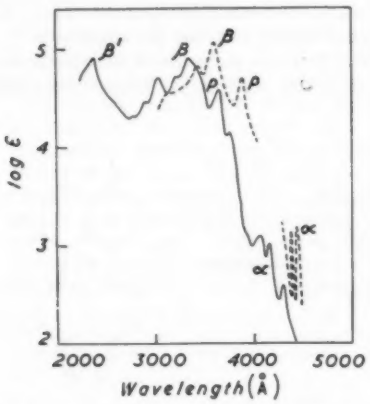


FIG. 2.

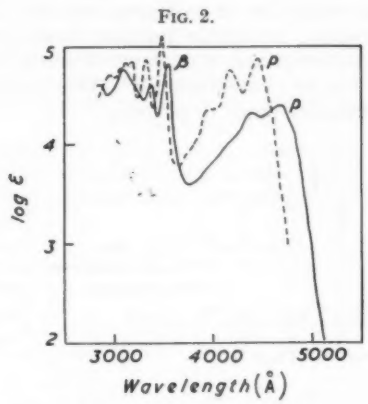


FIG. 1. *Absorption max.* (Å) *and* log ε (*in parentheses*) *of*: (——) 1 : 2-3 : 4-5 : 6-10 : 11-*tetrabenzoanthanthrene* (VI) *in trichlorobenzene*: α, 4300 (2·60), 4150 (3·01), 4050 (3·09), 3750 (4·15); *p*, 3650 (4·57); β, 3340 (4·89), 3200 (4·70); *in dioxan*, 3020 (4·70), 2900 (4·47); β', 2380 (4·91).
(– – – –) 1 : 12-2 : 3-4 : 5-6 : 7-8 : 9-10 : 11-*hexabenzocoronene* (III) *in trichlorobenzene*. Owing to the very low solubility the absolute intensities are uncertain: (log ε + *X*), *p*, 3875 (4·68); β, 3600 (5·06), 3425 (4·80). α-Bands were observed visually with a 100-cm. cell, 4440, 4380 (very sharp).

FIG. 2. *Absorption max.* (Å) *and* log ε (*in parentheses*) *of*: (——) 4 : 5-6 : 7-11 : 12-13 : 14-*tetrabenzoperopyrene* (II) *in benzene*; *p*, 4670 (4·40), 4420 (4·34); β, 3530 (4·83), 3375 (4·61), 3090 (4·78).
(— — —) 4 : 5-11 : 12-*dibenzoperopyrene in benzene*; *p*, 4450 (4·86), 4180 (4·74), 3980 (4·36); β, 3480 (5·10), 3320 (4·85), 3165 (4·83), 3110 (4·83), 2960 (4·70).

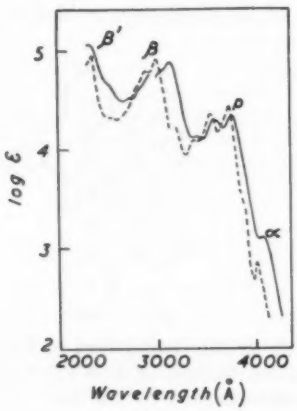


FIG. 3. *Absorption max.* (Å) *and* log ε (*in parentheses*) *of*: (——) *the phenyltribenzoperylene* (V) *in trichlorobenzene*: α, 4075 (3·12); *p*, 3775 (4·34), 3580 (4·30), 3400 (4·14); β, 3140 (4·89). *From* 3000 Å *in* n-*heptane*; β', 2340 (5·04).
(— — —) 1 : 12-2 : 3-10 : 11-*tribenzoperylene in trichlorobenzene*: α, 4010 (2·86); *p*, 3740 (4·45), 3540 (4·37), 3380 (4·11); *in* n-*heptane*, β, 3000 (4·92), 2880 (4·80), β', 2350 (4·96).

carbon (V) is closely related to that of 1 : 12-2 : 3-10 : 11-tribenzoperylene [1] (Fig. 3); the phenyl ring, being out of plane, has little influence on the absorption spectrum of the non-phenylated compound. The phenyl-compound (V) was cyclised to the tetrabenzanthanthrene (VI) in a sodium chloride–aluminium chloride melt. The pale yellow product showed the expected properties of a purely benzenoid hydrocarbon; it did not dissolve in cold sulphuric acid and showed strong phosphorescence of long life in solid solution in

dioxan at low temperature. The hydrocarbon (VI) (absorption spectrum; Fig. 1) fills the gap in the series between 1 : 12-2 : 3-10 : 11-tribenzoperylene and hexabenzocoronene.

The Table gives a comparison of the spectral changes in passing from benzene to hydrocarbons with 2, 3, 4, 5, 6, and 7 benzenoid rings, as indicated in formula (VII). This comparison is best made with the β-bands; the α-bands, which shift as do the β-bands, are

		Position				Shift				
	Number of benzenoid	First β-band		First *p*-band		First β-band		First *p*-band		
Hydrocarbon	rings	Å	Å$^{-\frac{1}{2}}$	Å	Å$^{-\frac{1}{2}}$	Å	Å$^{-\frac{1}{2}}$	Å	Å$^{-\frac{1}{2}}$	Ref.
Benzene	1	1790V 1819 corr.	42·65	2068A	45·48					*a*
						161	1·85	432	4·52	
Diphenyl	2	1980	44·50	2500H	50·00					
						59	6·20	340	3·29	
Triphenylene	3	2570A	50·70	2840A	53·29					*b*
						280	2·69	417	3·78	
Dibenzopyrene	4	2850H	53·39	3257H	57·07					*c*
						150	1·38	433	3·68	
Tribenzoperylene	5	3000H	54·77	3690H	60·75					*d*
						285	2·55	−106	−0·88	
Tetrabenzoanthanthrene (VI)	6	3340T 3285 corr.	57·32	3650T 3584 corr.	59·87					*e*
						252	2·16	223	1·78	
Hexabenzocoronene (III)	7	3600T 3537 corr.	59·48	3875T 3807 corr.	61·65					*e*

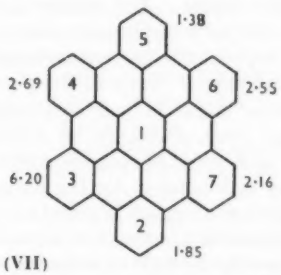
Solvent: V = vapour, A = *alcohol*, H = *heptane*, T = *trichlorobenzene*.

Corr.: corrected for heptane solution: vapour state ⟶ heptane = −900 cm.$^{-1}$; trichlorobenzene ⟶ heptane = +500 cm.$^{-1}$; alcohol ⟶ heptane = 0 cm.$^{-1}$.

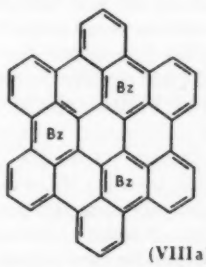
References: *a*, Scheibe, Povenz, and Lindstrom, *Z. phys. Chem.*, *B*, 1933, **20**, 283. *b*, Clar, *Spectrochim. Acta*, 1950, **4**, 116. *c*, Clar, *Ber.*, 1943, **76**, 613. *d*, Clar and Zander, *J.*, 1958, 1861. *e* this paper.

less suitable because in diphenyl the *p*-band is superimposed on the α-band. The *p*-bands involve the localisation of π-electrons in the excited state. Since this localisation takes place in different positions in different hydrocarbons, their comparison does not show any regularities (see Table 1).

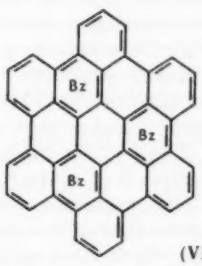
The differences, in Å or better Å$^{-\frac{1}{2}}$, the latter being a scale for reciprocal nuclear charges,[6] show the changing degree of electronic interaction between the benzenoid rings. The β-band of benzene shifts by 1·85 Å$^{-\frac{1}{2}}$ in passing to diphenyl as a result of the quasi-single bond or contact bond between the two rings. The transition to triphenylene brings a much bigger shift of 6·20 Å$^{-\frac{1}{2}}$. This could be related to the more highly conjugated structure (IXa) which, unlike (IXb), provides better electronic interaction between the three



(VII)



(VIIIa)



(VIIIb)

external rings through double bonds. The Kekulé structure (IXb) is also one of the eight possible structures contained in formula (IX). The three bonds linking the three external rings in triphenylene can therefore assume single- and double-bond character which is the characteristic of a true aromatic bond.

[6] Clar, "Aromatische Kohlenwasserstoffe," Springer-Verlag, 1952, pp. 25, 51; Clar and Willicks, *Chem. Ber.*, 1956, **89**, 743; Clar and Kühn, *Annalen*, 1956, **601**, 181; Boggiano and Clar, *J.*, 1957, 268.

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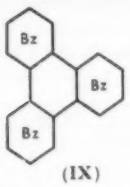
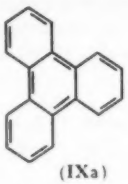
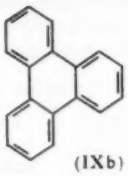
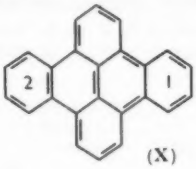
The fourth benzenoid ring in 1 : 2-6 : 7-dibenzopyrene (X) can be connected to structure (IXa) only by two single or contact bonds. Therefore only ring 1 or ring 2 can be linked



(IX)


(IXa)


(IXb)



(X)

to the diphenyl system by two double bonds in formula (X). This would produce a much smaller shift than in passing from diphenyl to triphenylene. It amounts to 2·69 Å$^{\frac{1}{2}}$ which is less than double the shift for the contact bond in diphenyl. Thus the two phenylene rings 1 and 2 in dibenzopyrene (X) show a strong asymmetric anellation starting from diphenyl which is quite different from the acene and phene series where the anellation per ring is constant [6] in units A$^{\frac{1}{2}}$. This is also the reason why dibenzopyrene (X) has not the properties of a dibenzotetracene.

Ring 5 in formula (VII) is connected to dibenzopyrene by two contact bonds; the shift associated with them decreases to 1·38 A$^{\frac{1}{2}}$. A similar decrease of the shift is observed in passing from diphenyl to terphenyl in comparison with the shift from benzene to diphenyl. Building up tetrabenzanthanthrene from tribenzoperylene [addition of ring 6 in formula (VII)] involves the formation of another two contact bonds which produce a shift of 2·55 Å$^{\frac{1}{2}}$, about the same as that for the formation of the bond between rings 3 and 4 in formula (VII).

The most striking feature of this comparison is the lack of any particular effect when the gap is filled with the formation of the hexagonally symmetrical hexabenzocoronene [*i.e.*, formation of bond between rings 6 and 7 in formula (VII)]. Although the seventh ring is connected through three contact bonds the shift is only 2·16 Å$^{\frac{1}{2}}$, corresponding to less than two contact bonds. There is no evidence for the tempting assumption of a rotation of π-electrons through the external frame of 15 alternating double bonds in Kekulé structures (VIIIa) and (VIIIb). Here the six central double bonds would be accommodated in a triphenylene system marked Bz. The 15 external double bonds in (VIIIa) and (VIIIb) alone should shift the β-band as far to the red as in heptaphene [7] which is obviously not the case.

Contrary to this, structure (VII) contains the frame of a cyclic *m*-sexiphenyl. It has been shown that the spectrally recorded conjugation in the *m*-polyphenyl series does not extend beyond diphenyl [8] which agrees well with the above shifts. The greater part of electronic interchange should therefore result from the six crossed *p*-terphenyl systems and go through the middle ring. This comparison does not support the current assumption that all Kekulé structures contribute equally to the ground state. Many of the possible Kekulé structures [like (VIIIa) and (VIIIb) with four benzenoid rings less than the maximum seven] with a higher degree of conjugation between rings have obviously no influence [except (IXa)] whilst the arrangement of double bonds in benzenoid rings is preferred. The assumption of contact bonds between them accounts satisfactorily for the observed shifts. The comparison also shows the clear difference between a contact bond which cannot become a double bond in terms of Kekulé structures (type found in the central bonds of diphenyl and perylene) and an aromatic bond which can become a single or a double bond (type found in the acenes and phenes).

Experimental

M. p.s were measured in evacuated capillaries. Microanalyses were by J. M. Cameron and his staff.

[7] Clar and Kelly, *J. Amer. Chem. Soc.*, 1954, **76**, 3502.
[8] Gillam and Hey, *J.*, 1939, 1170.

2 : 3-7 : 8-*Dibenzoperinaphthene Perbromide*.—Bromine (7·5 g.) in benzene (20 ml.) was added to the dibenzoperinaphthene (I) (5·0 g.) in benzene (100 ml.). The dark brown *perbromide* was filtered off, washed with benzene, and dried in a vacuum at 50° (yield 7·9 g.) (Found: C, 50·8; H, 2·8; Br, 46·8. $C_{21}H_{14}Br_2$ requires C, 49·8; H, 2·8; Br, 47·4%). It decomposed gradually with evolution of hydrobromic acid. When a solution of the perbromide in acetone was cooled dibenzoperinaphthene, m. p. 170°, crystallised in needles. In boiling acetic acid the perbromide formed a mixture of dibenzoperinaphthone, m. p. 208°, and dibenzoperinaphthene which could be separated by crystallisation from xylene and acetic acid. The perbromide melted at 153° with evolution of hydrobromic acid and resolidified immediately; the solid then contained tetrabenzoperopyrene (II). The perbromide gave up bromine when a suspension in nitrobenzene or carbon disulphide was titrated with aqueous sodium thiosulphate (potassium iodide–starch indicator) (Found: 1·6 atoms of Br/molecule in nitrobenzene; 1·8 in carbon disulphide).

4 : 5-6 : 7-11 : 12-13 : 14-*Tetrabenzoperopyrene* (II).—Dibenzoperinaphthene perbromide (3·15 g.) was melted in a vacuum at 153° (Found: loss, 1·38 g. Calc. for 3HBr: 1·51 g.). The powdered melt was sublimed at 400°/0·1 mm.; *tetrabenzoperopyrene* sublimed in orange prisms which were crystallised from trichlorobenzene and xylene (Found: C, 96·0; H, 4·1. $C_{42}H_{22}$ requires C, 95·8; H, 4·2%). It did not dissolve in cold concentrated sulphuric acid, melted at 481—482° with evolution of hydrogen (86% of the calculated volume was collected), and resolidified with formation of hexabenzocoronene (III).

1 : 12-2 : 3-4 : 5-6 : 7-8 : 9-10 : 11-*Hexabenzocoronene* (III).—(*a*) The crude molten tetrabenzoperopyrene was sublimed at 500°/0·1 mm. *Hexabenzocoronene* sublimed in pale brownish-yellow needles which were recrystallised from boiling pyrene. Hot 1-methylnaphthalene was added to the cooling solution to keep it liquid. Hexabenzocoronene was obtained in long flat needles which were resublimed (Found: C, 96·4; H, 3·5. $C_{42}H_{18}$ requires C, 96·5; H, 3·5%). It did not melt <700° and did not dissolve in concentrated sulphuric acid. It was very slightly soluble in trichlorobenzene. When this solution was cooled in liquid nitrogen and irradiated (mercury lamp) a very strong orange phosphorescence of long life appeared. The short-life blue phosphorescence of trichlorobenzene was easily masked by it.

(*b*) Dibenzoperinaphthene (I) (2·6 g.) and sulphur (0·64 g.; 2 atomic proportions) were powdered together. When the mixture was melted (at 220°) it evolved hydrogen sulphide and became solid. Xylene was added and the residue filtered off, washed, sublimed from copper at 500°/0·1 mm., and then recrystallised from boiling pyrene. The hydrocarbon was identical with the hexabenzocoronene described above. The yield was variable.

(*c*) A considerable amount of hexabenzocoronene was obtained when the distillation residue from the preparation of dibenzoperinaphthene [2] was powdered, sublimed, and crystallised as described above.

1′-*Phenyl*-1 : 12-2 : 3-10 : 11-*tribenzoperylene* (V).—**2 : 3-10 : 11**-Dibenzoperylene [1] (3 g.) and phenylacetylene (5 g.) were refluxed for 3 hr. More phenylacetylene (5 g.) was added and refluxing continued for 7 hr. The suspended dibenzoperylene gradually dissolved and yellow needles, changing to prisms, appeared. The viscous mixture was diluted with xylene (20 ml.), and the crystals (1·3 g.) filtered off. More (0·2 g.) were obtained by evaporation of the xylene and replacing it by ether. The *phenyltribenzoperylene* was crystallised from nitrobenzene–trichlorobenzene and twice from xylene. It formed pale yellow prisms, m. p. 354—356°, and did not dissolve in concentrated sulphuric acid (Found: C, 95·6; H, 4·4. $C_{36}H_{20}$ requires C, 95·5; H, 4·5%). It showed a strong orange-yellow phosphorescence in solid solution in dioxan cooled in liquid nitrogen.

1 : 2-3 : 4-5 : 6-10 : 11-*Tetrabenzanthanthrene* (VI).—Powdered phenyltribenzoperylene (0·3 g.) was added to a melt of sodium chloride (3 g.) and aluminium chloride (15 g.) at 120°. The temperature was raised to 140° and kept for 8 min. Decomposition of the melt with dilute hydrochloric acid gave a yellow precipitate which was filtered off and washed with hot water and ammonia. It sublimed almost completely at 400°/0·1 mm. The sublimate was crystallised twice from trichlorobenzene giving long flat greenish yellow needles, m. p. 434—436°, which did not dissolve in concentrated sulphuric acid (Found: C, 96·1; H, 4·3. $C_{36}H_{18}$ requires C, 96·0; H, 4·0%). They showed a strong yellow phosphorescence of long life in solid solution in dioxan cooled in liquid nitrogen.

One of us (M. Z.) thanks Rütgerswerke A.-G. for a scholarship.

UNIVERSITY OF GLASGOW. [*Received, April 28th*, 1958.]

29. *Fluorocyclohexanes. Part IV.*[1] 1H : 2H/4H- *and* 1H : 2H : 4H/-*Nonafluorocyclohexane* * *and Related Compounds.*

By R. Stephens, J. C. Tatlow, and E. H. Wiseman.

Two nonafluoro*cyclo*hexanes, b. p. 107° (I) and 124° (II), isolated from the polyfluoro*cyclo*hexane mixture made by the fluorination of benzene, have been studied by methods making extensive use of gas chromatography on both analytical and preparative scales. Six unsaturated products, obtained from the isomer (I) by dehydrofluorination with aqueous alkali, were identified as 1*H*-heptafluoro*cyclo*hexa-1 : 4-diene, 1*H*- and 2*H*-heptafluoro*cyclo*hexa-1 : 3-diene, and 1*H* : 5*H*-, 3*H* : 4*H*/-, and 4*H* : 5*H*/-octafluoro*cyclo*hexene. Compound (I) was thus 1*H* : 2*H*/4*H*-nonafluoro*cyclo*hexane; this was confirmed by further fluorination with cobaltic fluoride to the known 1*H* : 2*H*/-, 1*H*/3*H*-, and 1*H*/4*H*-decafluoro*cyclo*hexane. With alkali, compound (II) gave the same six unsaturated products, together with 1*H* : 4*H*-octafluoro*cyclo*hexene, and fluorination afforded the three *cis*-decafluoro-compounds: it was therefore 1*H* : 2*H* : 4*H*/-nonafluoro*cyclo*hexane. All four 1*H* : 2*H* : 4*H*-nonafluoro-compounds were synthesised from 4*H*-nonafluoro*cyclo*hexene by addition of chlorine, followed by reduction with lithium aluminium hydride. A *cyclo*alkene, 1*H* : 2*H* : 4*H*-heptafluoro*cyclo*hexene (b. p. 106°), was obtained in very small yield from the fraction of the polyfluoro-mixture affording compound (I).

Isolation of Compounds.—The complete characterisation of two 1*H* : 2*H* : 4*H*-nonafluoro*cyclo*hexanes has been reported recently.[1] From the same source, the mixture of cyclic polyfluoro-compounds[1-4] obtained by the treatment of benzene in the vapour phase with cobaltic fluoride at about 150°, two new isomeric nonafluoro-compounds (I and II) and a heptafluoro*cyclo*hexene (III) have been isolated and identified. Investigations of them and various derived compounds are reported in this paper.

Two of the new compounds to be described (I and III) were contained in a major fraction, b. p. 106—107°, obtained by fractional distillation controlled by analytical gas chromatography,[5,6] of the polyfluoro-mixture remaining after removal[1] of 1*H* : 4*H*/2*H*-(VII) and 1*H*/2*H* : 4*H*-nonafluoro*cyclo*hexane (VIII) (b. p. 92° and 101° respectively). However, this fraction, though inseparable further by fractional distillation, was shown by analytical gas chromatography to be a mixture of two components, one in considerable excess. The constituents were separated by preparative-scale gas chromatography,[7] the minor one (III) with the lower retention time being a liquid heptafluoro*cyclo*hexene (b. p. 106°) and the major component (I) a nonafluoro*cyclo*hexane (b. p. 107°, m. p. 35°).

Further distillation of the original polyfluoro*cyclo*hexane mixture having b. p. >107° yielded a major fraction of b. p. 118°, which was 1*H* : 4*H*/2*H* : 5*H*-octafluoro*cyclo*hexane,[8,9] and then, over the boiling range of 120—127°, a mixture of six compounds was obtained but in small yield. This could be separated[9] only by preparative-scale gas chromatography and one of the pure compounds isolated (II) had b. p. 124°, m. p. 26°, and was

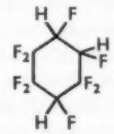
* The stereochemical nomenclature used here and in other Parts follows that suggested for the inositols (Angyal and Macdonald, *J.*, 1952, 686; Whiffen, *Chem. and Ind.*, 1956, 964). The American convention, adopted also in the *Journal* (see *J.*, 1952, 5059), governing the use of *H* to denote hydrogen in polyhalogeno-compounds contains the limitation that the ratio of hydrogen to halogen shall not " ordinarily " exceed 1 : 3. To preserve uniformity of names in the present series of papers this limitation is not applied to the relatively small proportion of compounds affected.

[1] Part III, Godsell, Stacey, and Tatlow, *Tetrahedron*, 1958, **2**, 193.
[2] Barbour, Mackenzie, Stacey, and Tatlow, *J. Appl. Chem.*, 1954, **4**, 341, 347.
[3] Smith and Tatlow, *J.*, 1957, 2505.
[4] Evans, Godsell, Stephens, Tatlow, and Wiseman, *Tetrahedron*, 1958, **2**, 183.
[5] Evans and Tatlow, *J.*, 1955, 1184.
[6] *Idem*, " Vapour Phase Chromatography," (Editor Desty), Butterworths, London, 1956, p. 256.
[7] Evans, Massingham, Stacey, and Tatlow, *Nature*, 1958, **182**, 591.
[8] Stephens and Tatlow, *Chem. and Ind.*, 1957, 821.
[9] Nield, Stephens, and Tatlow, following paper.

another nonafluoro*cyclo*hexane. This (II) and the other stereoisomeric nonafluoro-compounds (I, VII, and VIII) were all synthesised together by an alternative method (see below).

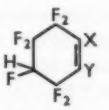
The compounds (I—III) were identified by dehydrofluorination, the mixtures of unsaturated products being separated by preparative-scale gas chromatography. The columns used before [5,6] and a larger unit [7] were used, the latter, a tube 16 ft. × 7·5 cm. being capable of handling charges of 10—25 g. of most mixtures. The dehydrofluorination products were characterised by oxidation and further dehydrofluorination. Considerable use was also made of infrared spectroscopy, not only for proving the identity of known compounds with authentic samples, but also for confirmation of the types of double bond (Burdon and Whiffen [10]) and ⩾CH groups (Steele and Whiffen [11]) present.

*Characterisation of the Heptafluoro*cyclo*hexene of b. p.* 106°.—This substance (III), the minor constituent of the fraction of b. p. 106—107°, was shown by analysis to have the formula $C_6H_3F_7$, and was the first unsaturated compound to be found in the product of the benzene–cobaltic fluoride reaction. It was oxidised by aqueous potassium permanganate to the known 3*H*-heptafluoroadipic acid,[2,5,13] and had an infrared spectrum consistent [10,11] with the presence of a >CH=CH< double bond and a hydrogen substituent



(I) 1Ha: 2He/4Ha

(II) 1He: 2Ha: 4Ha/

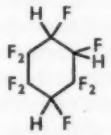


(III) X = Y = H

(IV) X = F, Y = H

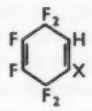
(V) X = Y = F

(VI) X = H, Y = F



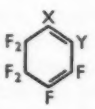
(VII) 1Ha: 4He/2Ha

(VIII) 1Ha/2Ha: 4Ha



(IX) X = H

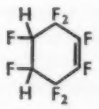
(X) X = F



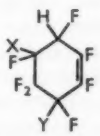
(XI) X = Y = H

(XII) X = H, Y = F

(XIII) X = F, Y = H



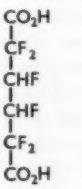
(XIV) 4H: 5H/



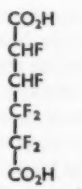
(XV) X = H, Y = F

3H: 4H/

(XVI) X = F, Y = H



(XVII)



(XVIII)

on the β-carbon atom. Dehydrofluorination of this olefin (III) afforded a mixture, which was shown by analytical gas chromatography to contain two compounds (IX and XI). These were isolated by preparative-scale gas chromatography, each being a new hexafluoro*cyclo*hexadiene. Oxidation was carried out with potassium permanganate in dry acetone, which converts [12] fluoro-olefins into carboxylic acids smoothly and rapidly. Difluoromalonic acid was obtained from one diene (IX) and tetrafluorosuccinic acid from the other (XI). Ultraviolet and infrared spectra confirmed the presence of a 1 : 4-diene system in (IX) and a 1 : 3-diene system in (XI), both with two hydrogen atoms carried on one double bond. Thus, the parent olefin (III) must have been 1*H* : 2*H* : 4*H*-heptafluoro-*cyclo*hexene, and the derived dienes were 1*H* : 2*H*-hexafluoro*cyclo*hexa-1 : 4- (IX) and -1 : 3-diene (XI).

The *cyclo*hexene (III) had been reported before by Fear and Thrower [13] as one of the major products of the fluorination of benzene with manganese trifluoride. This fluorination was repeated by us, and the previous results confirmed: the product obtained was identical

[10] Burdon and Whiffen, *Spectrochim. Acta*, 1958, **12**, 139.
[11] Steele and Whiffen, *Tetrahedron*, 1958, **3**, 181.
[12] Burdon and Tatlow, *J. Appl. Chem.*, 1958, **8**, 293.
[13] Fear and Thrower, *ibid.*, 1955, **5**, 353; Fear, Thrower, and Veitch, *ibid.*, p. 589.

XUM

with that from the reaction with cobaltic fluoride. Manganese trifluoride provides the easier route to the compound.

Characterisation of the Nonafluorocyclohexane of b. p. 107°.—The substance (I) was dehydrofluorinated with aqueous potassium hydroxide under comparatively mild conditions (contrast the known [1] isomers), and gave a mixture which was shown by analytical gas chromatography to contain, besides a little starting material, six products (IV, X, XII—XV), which were isolated pure by preparative-scale gas chromatography. The first three to emerge from the column were dienes and had gas-chromatographic retention times and infrared spectra identical with those of 1*H*-heptafluoro*cyclo*hexa-1 : 4-diene (X) and 1*H*- and 2*H*-heptafluoro*cyclo*hexa-1 : 3-diene (XII and XIII) respectively. These were characterised in the earlier work,[1] but for the conjugated dienes it was not possible to distinguish between the two compounds (b. p. 72° and 76°) obtained. Though each could have had either formula (XII) or formula (XIII), and no other, it was impossible at that stage to allocate the structures more precisely.

An attempt was made to decide between the two possibilities by controlled addition of fluorine to each of the dienes by passage over cobaltic fluoride at only slightly elevated temperatures. This had been attempted previously [1] but the products were not then identified conclusively. By normal 1 : 2- and 1 : 4-additions, only the 1*H*-1 : 3-diene should give 4*H*-nonafluoro*cyclo*hexene (V) among the *cyclo*hexene products, but it appeared to be formed together with unidentified substances from both. When the reactions were repeated, the lower-boiling 1 : 3-diene (b. p. 72°) was passed over cobaltic fluoride at 55—65° in the small static reaction vessel described before,[4] to give a mixture of seven compounds. These were separated gas-chromatographically and identified by retention times and by infrared spectroscopy as perfluoro*cyclo*hexane, decafluoro*cyclo*hexene, undecafluoro*cyclo*hexane, 1*H*-heptafluoro*cyclo*hexa-1 : 4-diene (X), and 1*H*-, 3*H*-, and 4*H*- (V) nonafluoro*cyclo*hexene. The isomeric 1 : 3-diene of b. p. 76° gave a very similar pattern of products, only decafluoro*cyclo*hexene being absent. Thus, the 4*H*-*cyclo*hexene (V) was in fact formed in both cases, as was a 1 : 4-diene (X). Clearly, no progress had been made in elucidating the structures of the 1 : 3-dienes and a new problem had been posed. However, other work [14] in this Department has since shown that, when brought into contact with metals or metallic fluorides at elevated temperatures, cyclic fluoro-1 : 3- and -1 : 4-dienes are interconverted: possibly equilibria are established. It seems that in the cobaltic fluoride vessel some of the 1 : 3-diene must rearrange thus to the 1 : 4-isomer by contact with a metallic fluoride (copper fluoride in the preheating system or nickel or cobalt fluoride near the inlet) before being saturated with fluorine. Additions to the mixture of 1 : 3- and 1 : 4-dienes can then give all the other products found.

The fourth product (IV) of the original dehydrofluorination was an octafluoro*cyclo*hexene. On oxidation with permanganate in acetone, the known 3*H*-heptafluoroadipic acid was obtained. Infrared spectroscopy also indicated the presence of a $\rangle CH{=}CF\langle$ double bond, and of hydrogen at the β-position. Reaction with cobaltic fluoride in the small static reaction vessel gave two decafluoro*cyclo*hexanes, shown by gas chromatography and infrared spectroscopy to be the 1*H*/3*H*- and 1*H* : 3*H*/-isomers. The structure of the product (IV) was thus established as 1*H* : 5*H*-octafluoro*cyclo*hexene.

The isolation of this compound (IV) enabled the structures of the two conjugated dienes (XII and XIII), mentioned above, to be unequivocally allocated. On dehydrofluorination, by normal elimination processes it can give only two dienes, 1*H*-heptafluoro*cyclo*hexa-1 : 4-diene (X) and 2*H*-heptafluoro*cyclo*hexa-1 : 3-diene (XIII). Experimentally, the *cyclo*hexene (IV) reacted only slowly with aqueous alkali but gave two products, the first being the unconjugated diene (X). The other was identical with the conjugated diene of longer gas-chromatographic retention time and higher boiling point (76°), which must therefore be the 2*H*-compound (XIII).

The fifth product (XIV) of the dehydrofluorination of compound (I) was also an

[14] Gething, Patrick, and Tatlow, unpublished observations.

octafluoro*cyclo*hexene. Oxidation of it afforded a hexafluoroadipic acid which was degraded by aqueous alkaline potassium permanganate to difluoromalonic acid and so it had a 3*H* : 4*H*-structure (XVII). Dehydrofluorination of the parent (XIV) with alkali gave the 1*H*-1 : 4-diene (X) and hexafluorobenzene. Infrared spectroscopy confirmed the presence of a >CF=CF< group and the absence of an α-hydrogen atom and so the compound (XIV) must have been a 4*H* : 5*H*-octafluoro*cyclo*hexene. However, it differed from the known [1] 4*H*/5*H*-compound, and the derived acid (XVII) differed from (±)-3*H* : 4*H*-hexafluoroadipic acid.[1] The compound (XIV) must therefore have been the 4*H* : 5*H*/-isomer (it was dehydrofluorinated more readily than the 4*H*/5*H*-compound). This was confirmed in two ways. First, attempts to resolve the dibrucine salt of the derived hexafluoroadipic acid (XVII) were unsuccessful. Secondly, reaction of the *cyclo*hexene (XIV) with cobaltic fluoride afforded only undeca- and 1*H* : 2*H*/-deca-fluoro-*cyclo*hexane.[3,4] Compound (XIV) was therefore 4*H* : 5*H*/-octafluoro*cyclo*hexene and the derived acid (XVII) was *meso*-3*H* : 4*H*-hexafluoroadipic acid.

The sixth product obtained from the dehydrofluorination of the nonafluoro*cyclo*hexane (I) was an octafluoro*cyclo*hexene (XV) to which fluorine was added by cobaltic fluoride giving 1*H* : 2*H*/-decafluoro*cyclo*hexane.[3,4] Oxidation of the *cyclo*hexene (XV) gave a hexafluoroadipic acid (XVIII). This acid was degraded by aqueous alkaline permanganate to tetrafluorosuccinic acid, but it differed from the known [1] (±)-*threo*-2*H* : 3*H*-hexafluoroadipic acid. The compound (XV) was therefore 3*H* : 4*H*/-octafluoro*cyclo*hexene (infrared spectroscopy confirmed the >CF=CF< group and the presence of hydrogen α and β to it), and the acid (XVIII) was (±)-*erythro*-2*H* : 3*H*-hexafluoroadipic acid. Dehydrofluorination of the *cyclo*hexene (XV) gave a mixture shown by analytical gas chromatography to contain 5 components, one of them starting material. Three others were the 1*H*- and 2*H*-1 : 3-dienes (XII) and (XIII) (arising from 1 : 2-elimination) and hexafluorobenzene [arising from a 1 : 4-elimination of hydrogen and fluorine as expected from the structure of compound (XV)]. The fourth product was formed in too small quantity for conclusive proof of its structure: preliminary experiments indicate that it is a 3*H* : 6*H*-octafluoro-*cyclo*hexene (XVI) which could be formed from the 3*H* : 4*H*/-compound (XV) by a prototropic change. If this is true it is the first example of such an effect in fluoro*cyclo*hexanes. It is also of interest that this *cyclo*hexene (XV) has an abnormally long retention time in gas chromatography, even for a compound with a *cis*-1*H* : 2*H*-arrangement: [4] it is retained much longer than the 4*H* : 5*H*/-isomer (XIV) (cf. the 3*H*/4*H*- and 4*H*/5*H*-analogues [1]). The refractive index of compound (XV) is also high, and the association of *cis*-1 : 2-hydrogen and an adjacent double bond obviously gives rise to abnormal properties.

The structures established as described above for each of the products of dehydrofluorination of the nonafluoro*cyclo*hexane (I) showed that it had hydrogen at positions 1, 2, and 4. Without profound rearrangements, a 1*H* : 2*H* : 3*H*-compound could not give rise to the 1 : 4-diene (X) or the 4*H* : 5*H*-ene (XIV), whilst from a 1*H* : 3*H* : 5*H*-structure none of the products should be obtained.

Further, in both of the *cyclo*hexenes (XIV) and (XV), the 1*H* : 2*H*-system was proved conclusively to be *cis*, since the only product of saturation of the double bonds by fluorine was the known 1*H* : 2*H*/-decafluoro*cyclo*hexane. Hence, if it is assumed that in the more stable conformation of a *cyclo*hexane of this general type, the hydrogen atoms, being smaller, preferentially occupy *axial* positions where possible,[3] the nonafluoro-compound (I) could only be either the 1*Ha* : 2*He*/4*Ha*- or the 1*He* : 2*Ha* : 4*Ha*/-stereoisomer. In the cases of the two nonafluoro-compounds (VII) and (VIII) with 1*Ha*/2*Ha*-systems, studied earlier,[1] monounsaturated compounds were formed only from eliminations at the isolated hydrogen atom, even when this was *equatorial*, and in both cases elimination was relatively slow. This paralleled the difficulty in dehydrofluorination [3] of 1*H*/2*H*-decafluoro*cyclo*-hexane compared with that of its five isomers. The 1*H* : 2*H*/-decafluoro-analogue however was dehydrofluorinated at a rate qualitatively comparable [3,4] with those of compounds possessing a >CHF group (with an *axial* hydrogen) flanked by two $>CF_2$ groups. This

is to be expected; it seems likely that the arrangement $>CF_2 \cdot CHF \cdot CHF \cdot CF_2<$ has hydrogen atoms which are less acidic than the one in $>CF_2 \cdot CHF \cdot CF_2<$, but that fluorine in the group >CHF is rather less tightly bound than in $>CF_2$. If the preferred bimolecular *trans*-elimination [15] can operate entirely within the system >CHF·CHF< to give >CH=CF<, as in the case of the *cis*-1*H* : 2*H*-decafluoro-compound, the reactivity is then qualitatively comparable with that of $>CF_2 \cdot CHF \cdot CF_2<$ since both effects are involved and roughly cancel out. With the *trans*-1*H* : 2*H*-isomer however the preferred process can only occur " outwards," *i.e.*, the fluorine must come from the more stable group ($>CF_2$), so that the overall reactivity is lowered. Alternatively, the " inwards " elimination can proceed by a less favoured mechanism. In either case elimination from the 1*H*/2*H*-system should occur only slowly.

With 1*H* : 2*H* : 4*H*-nonafluoro*cyclo*hexanes possessing *cis*-1*H* : 2*H*-systems, it appears from the foregoing discussion that, upon dehydrofluorination, *cyclo*hexenes should be obtained by relatively easy eliminations, the hydrogen coming from either the 4- or the 1 : 2-positions. Experimentally, from compound (I), elimination of hydrogen from $C_{(4)}$ occurred in both possible directions, to give two olefins with >CF=CF< double bonds (XIV and XV) (in all *ca.* 65% of the monounsaturated dehydrofluorination products), but elimination from the 1 : 2-positions occurred in only one direction, to give exclusively the 1*H* : 5*H*-*cyclo*hexene (IV) (*ca.* 35%). The reactions were qualitatively more rapid than for the *trans*-1*H* : 2*H*-stereoisomers.[1] This suggested strongly that the hydrogen on position 2 of the parent compound (I), being the one retained in the only elimination from the 1 : 2-system, was *equatorial*. Therefore, the precursor (I) was 1*H*a : 2*H*e/4*H*a-nonafluoro*cyclo*hexane.

This allocation of structure was confirmed completely by further fluorination of the fluorohydrocarbon (I) with cobaltic fluoride. Three known decafluoro*cyclo*hexanes were obtained, identical with authentic specimens.[4] They were the 1*H* : 2*H*/- (b. p. 91°), the 1*H*/4*H*- (b. p. 78°), and the 1*H*/3*H*-isomer (b. p. 78°).

*Characterisation of the Nonafluoro*cyclo*hexane of b. p.* 124°.—There should be four stereoisomeric 1*H* : 2*H* : 4*H*-nonafluoro*cyclo*hexanes, and the remaining one was isolated first from a synthesis which gave all four together. 4*H*-Nonafluoro*cyclo*hexene (V), a product [4,5] of the dehydrofluorination of 1*H* : 3*H*- and 1*H* : 4*H*-decafluoro*cyclo*hexanes, was treated with chlorine under ultraviolet irradiation. The adduct was not isolated, but was reduced directly with lithium aluminium hydride in diethyl ether, which readily replaces [16,17] chlorine in a chlorofluorocarbon by hydrogen. The product was shown by analytical gas chromatography to contain four components, which were isolated pure by preparative-scale gas chromatography. They were, in order of emergence from the column, the known nonafluoro*cyclo*hexanes 1*H* : 4*H*/2*H* (b. p. 92°; VII), 1*H* : 2*H*/4*H* (b. p. 107°; I), 1*H*/2*H* : 4*H* (b. p. 101°; VIII), and a new compound (b. p. 124°; II). The last was shown by infrared spectroscopy to be identical with the material subsequently isolated in small amounts as described earlier from a minor fraction of the polyfluoro*cyclo*hexane mixture. It is of interest, that as in the analogous reactions [3] with decafluoro*cyclo*hexene, the major part of the hydrofluorocarbon product had the *cis*-1*H* : 2*H*-arrangement. This suggests again a predominantly *cis*-addition of chlorine and retention or inversion of configuration in the reduction by lithium aluminium hydride.

That this compound (II) had the expected 1*H* : 2*H* : 4*H*/-configuration was proved by further fluorination with cobaltic fluoride. Three decafluoro*cyclo*hexanes were obtained, and were shown to be the known [4] 1*H* : 2*H*/- (b. p. 91°), 1*H* : 3*H*/- (b. p. 89°), and 1*H* : 4*H*/-isomer (b. p. 86°). Dehydrofluorination of the 1*H* : 2*H* : 4*H*/-nonafluoro-compound (II) was carried out also, and gave seven products which were isolated by gas chromatography. Six of them were the same compounds (IV, X, XII—XV) as had been obtained from the

[15] Ingold, " Structure and Mechanism in Organic Chemistry," Bell, London, 1953, p. 419.
[16] Tatlow and Worthington, *J.*, 1952, 1251.
[17] Roylance, Tatlow, and Worthington, *J.*, 1954, 4426.

dehydrofluorination of the stereoisomeric nonafluoro-compound (I). The seventh was another octafluoro*cyclo*hexene (VI), which was identified by oxidation and addition of fluorine. The former reaction afforded the well-known 3*H*-heptafluoroadipic acid, infrared spectroscopy confirming the presence of a >CH=CF< double bond. By reaction with cobaltic fluoride to saturate this bond, two known [4] decafluoro*cyclo*hexanes were formed. They were the 1*H*/4*H*- and the 1*H* : 4*H*/-isomer. Compound (VI) must therefore have been 1*H* : 4*H*-octafluoro*cyclo*hexene. Fear and Thrower [13] had previously isolated this from the reaction of benzene with manganic fluoride. They had shown that it was either 1*H* : 5*H*- (IV) or 1*H* : 4*H*-octafluoro*cyclo*hexene (VI) (or a mixture of the two). From the fluorination with manganese trifluoride mentioned above we also obtained their compound. It was different from the 1*H* : 5*H*-isomer (IV) described earlier, but was now shown to be identical with the 1*H* : 4*H*-*cyclo*hexene (VI). Dehydrofluorination of this product (VI) provided the final proof of the structures of the dienes (XII and XIII), since there were obtained, in accordance with the earlier results, the 1 : 4-diene (X) and the conjugated diene of lower gas-chromatographic retention time and with b. p. 72°, identical with compound (XII) described earlier.

It is at first sight curious that, whereas the nonafluoro-compound (I) gives exclusively 1*H* : 5*H*-octafluoro*cyclo*hexene (IV) by elimination of hydrogen fluoride from positions 1 and 2, the stereoisomer (II) affords both 1*H* : 4*H*- (VI) and 1*H* : 5*H*- (IV) *cyclo*hexene in comparable amounts. In both cases reaction occurred under mild conditions. The absence of olefin (VI) from the dehydrofluorination products of the nonafluoride (I) makes the direct elimination of *equatorial* hydrogen very unlikely, whilst its behaviour on further reaction with alkali rules out the possibility that it might be formed exclusively from compound (II) and itself rearrange to give olefin (IV).

Because of their relative atomic sizes, comparatively small non-bonded interactions can be introduced into *cyclo*hexane derivatives in which fluorine progressively replaces hydrogen (there can be little overall strain in perfluoro*cyclo*hexane). However, on general conformational grounds, one form (1*H*a : 2*H*e/4*H*a) of the nonafluoro-compound (I) should be more stable than the other (1*H*e : 2*H*a/4*H*e), since presumably 1a : 3a F–F interactions, of which the latter has more, introduce most strain. However, in the case of isomer (II), the two conformations (1*H*e : 2*H*a : 4*H*a and 1*H*a : 2*H*e : 4*H*e) differ much less in their total interactions, so that they should have approximately equal stabilities. These conclusions are in accordance with the experimental results. Isomer (I) gives the *cyclo*hexene (IV) by an orthodox *trans*-elimination, the hydrogen retained being the original equatorial one, whilst from isomer (II) each of the two nearly equivalent forms gives rise to its own (different) *cyclo*hexene.

Experimental

Characterisation of Acids obtained as Oxidation Products.—*cyclo*Hexenes were oxidised [12] to acids by potassium permanganate in acetone. The known acids difluoromalonic,[18] tetrafluorosuccinic,[16,19] and 3*H*-heptafluoroadipic [5] were characterised as dianilinium and di-(*S*-benzylthiuronium) salts. Each sample had a correct elemental analysis and the m. p. was within 2° of the reported value. The yields quoted are those of the analytically pure salts.

Gas Chromatography.—Analytical work was carried out in columns 2 m. long × 4 mm. diameter packed with dinonyl phthalate–kieselguhr (1 : 2) and run at 93° with a nitrogen flow rate of 1·1 l./hr. In preparative-scale work two columns were used. Column A was 488 cm. long × 30 mm. diameter and was similarly packed; it was normally run at 100° with a nitrogen flow rate of 10 l./hr. Column B was 488 cm. long × 75 mm. diameter; it had the same packing and was run at 100° with a nitrogen flow rate of 49 l./hr. After preparative-scale separations each fraction obtained was distilled from the trap *in vacuo*.

[18] Evans and Tatlow, *J.*, 1954, 3779.
[19] Buxton and Tatlow, *J.*, 1954, 1177.

XUM

Infrared Measurements.—These were made in the vapour state in a 10·1 cm. cell over the range 650—3500 cm.$^{-1}$ with a Perkin-Elmer double-beam spectrometer with rock-salt prisms. The spectra for the new compounds described have been deposited in the Documentation of Molecular Spectra issued by Butterworths.

Isolation of 1H : 2H/4H- *and* 1H : 2H : 4H/-*Nonafluorocyclohexane and* 1H : 2H : 4H-*Heptafluorocyclohexene.*—Fractional distillation controlled by analytical gas chromatography of the partly fluorinated *cyclo*hexane mixture having b. p. >101° gave a fraction with b. p. 106—107° (*ca.* 5% of the original polyfluorinated mixture), which was resolved by analytical gas chromatography into two components. Separation of the mixture (4·0 g.) in the preparative-scale gas chromatography column A afforded: (i) 1*H* : 2*H* : 4*H*-heptafluoro*cyclo*hexene (0·12 g.), b. p. 106°, n_D^{21} 1·3362 (Found: C, 34·9; H, 1·5. Calc. for $C_6H_3F_7$: C, 34·6; H, 1·45%), for which Fear and Thrower [13] gave b. p. 105—106°, n_D^{20} 1·335; and (ii) 1H : 2H/4H-*nonafluoro*cyclo*hexane* (3·60 g.), b. p. 107°, m. p. 34—35°, n_D^{44} 1·3090 (Found: C, 29·5; H, 1·3; F, 69·2. $C_6H_3F_9$ requires C, 29·3; H, 1·2; F, 69·5%).

After removal of material of b. p. 107·5—120°, mainly 1*H* : 4*H*/2*H* : 5*H*-octafluoro*cyclo*hexane,[9] b. p. 118°, there followed a mixed intermediate fraction, b. p. 120—127° (*ca.* 0·5% of the original mixture). From this there was isolated by preparative-scale gas chromatography as described elsewhere,[9] 1H : 2H : 4H/-*nonafluoro*cyclo*hexane*, b. p. 124°, m. p. 24—26°, n_D^{29} 1·3231 (Found: C, 29·7; H, 1·3%).

The 1*H* : 2*H*/4*H*-isomer gave peak No. 10 in the table of gas-chromatography results given earlier.[3] The 1*H* : 2*H* : 4*H*/-isomer, being a very small component and of long retention time under the conditions used, was not shown.

Dehydrofluorination of 1H : 2H : 4H-*Heptafluorocyclohexene.*—The olefin (3·52 g.; b. p. 106°), potassium hydroxide (15 g.), and water (15 c.c.) were boiled together for 4 hr. The organic phase (2·69 g.) was separated, washed with water, and dried ($MgSO_4$). Analytical gas chromatography showed 3 peaks. Separation in the preparative-scale column A afforded: (i) 1H : 2H-*hexafluoro*cyclo*hexa*-1 : 4-*diene* (1·14 g.), b. p. 83—84°, n_D^{19} 1·3417 (Found: C, 38·4; H, 1·4. $C_6H_4F_6$ requires C, 38·3; H, 1·1%): (ii) 1H : 2H-*hexafluoro*cyclo*hexa*-1 : 3-*diene* (0·64 g.), n_D^{22} 1·3529 (Found: C, 38·3; H, 1·1%); which decomposed rapidly in air; and (iii) 1*H* : 2*H* : 4*H*-heptafluoro*cyclo*hexene (0·63 g.), b. p. 106°. By longer refluxing it was possible to destroy all the parent *cyclo*hexene.

Characterisation of 1H : 2H-*Hexafluoro*cyclo*hexa*-1 : 4-*diene.*—(a) *Oxidation.* The diene (0·54 g.; b. p. 83—84°), potassium permanganate (2 g.), and dry acetone (400 c.c.), shaken together at room temperature for ½ hr., yielded difluoromalonic acid (78%).

(b) *Spectroscopy.* The diene showed two infrared >C=C< bands (1688 and 1770 cm.$^{-1}$), suggesting two hydrogen atoms on one double bond of a 1 : 4-diene. A >C–H band at 3087 cm.$^{-1}$ was due to =C–H only. No selective ultraviolet absorption was shown in the range 2400—3000 Å.

Characterisation of 1H : 2H-*Hexafluoro*cyclo*hexa*-1 : 3-*diene.*—(a) *Oxidation.* The diene (0·29 g.), oxidised with potassium permanganate (1 g.) in dry acetone (200 c.c.), afforded tetrafluorosuccinic acid (60%).

(b) *Spectroscopy.* Two >C=C< bands were shown in the infrared spectrum, at 1734 and 1635 cm.$^{-1}$. In the ultraviolet region there was a band at 2520 Å ($\varepsilon \sim 6300$) (0·57 g./l. in ether).

Other Reactions of 1H : 2H : 4H-*Heptafluorocyclohexene.*—(a) *Oxidation.* The compound (5·62 g.; b. p. 106°), potassium permanganate (12 g.), and water (50 c.c.) were boiled together for 23 hr. Isolation as usual yielded 3*H*-heptafluoroadipic acid, which was characterised as the dianilinium salt (7·33 g.).

(b) *Spectroscopy.* The compound showed a characteristically [10] very weak –HC=CH– infrared band at 1682 cm.$^{-1}$ and a >C–H band at 2981 cm.$^{-1}$ typical of β-hydrogen. No selective ultraviolet absorption was shown in the range 2400—3000 Å.

Dehydrofluorination of 1H : 2H/4H-*Nonafluorocyclohexane.*—The nonafluoro-compound (50·0 g.; b. p. 107°), potassium hydroxide (50·0 g.), and water (75 c.c.) were shaken together at 15° for 7 hr. The organic phase (41·6 g.) was separated, washed with water, and dried ($MgSO_4$). Analytical gas chromatography showed 7 peaks. Separation of part of the mixture (17·50 g.) in the large preparative-scale gas chromatography column B afforded: (A) 1*H*-heptafluoro*cyclo*hexa-1 : 4-diene (0·05 g.); (B) 1*H*-heptafluoro*cyclo*hexa-1 : 3-diene (0·02 g.); (C) 2*H*-heptafluoro*cyclo*hexa-1 : 3-diene (0·03 g.); (D) 1*H* : 5*H*-*octafluorocyclohex*-1-*ene* (4·65 g.), b. p. 85°, n_D^{21} 1·3260 (Found: C, 32·1; H, 1·0. $C_6H_2F_8$ requires C, 31·9; H, 0·9%); (E)

4H : 5*H*/-*octafluorocyclohexene* (2·55 g.), b. p. 99°, n_D^{21} 1·3234 (Found: C, 32·0; H, 0·9; F, 66·8. $C_6H_2F_8$ requires C, 31·9; H, 0·9; F, 67·2%); (F) unchanged 1*H* : 2*H*/4*H*-nonafluorocyclohexane (0·55 g.); and (G) 3H : 4H/-*octafluorocyclohexene* (6·01 g.), b. p. 116°, n_D^{21} 1·3390 (Found: C, 32·3; H, 1·0; F, 66·8%). The relative proportions of the products were varied by alteration of the reaction conditions, more vigorous treatment removing all starting material and increasing the amounts of products (A)—(C) at the expense of (F) and (G). Small quantities of hexafluorobenzene [20] were formed also from these *cyclo*hexenes. Compound (D) was relatively resistant to further dehydrofluorination except under drastic conditions.

Products (A), (B), and (C) had infrared spectra respectively identical with those of the dienes (i), (ii), and (iii) obtained [1] by dehydrofluorination of 1*H* : 4*H*/2*H*- and 1*H*/2*H* : 4*H*-nonafluoro*cyclo*hexane.

Characterisation of 1H : 5H-*Octafluorocyclohexene*.—(a) *Oxidation*. This compound (0·53 g.; b. p. 85°), oxidised by potassium permanganate (0·40 g.) in dry acetone (100 c.c.), gave 3*H*-heptafluoroadipic acid (54%).

(b) *Dehydrofluorination*. The *cyclo*hexene (2·31 g.), potassium hydroxide (10 g.), and water (10 c.c.) were boiled together for 7 hr. After being washed with water and dried ($MgSO_4$), the product (1·37 g.) showed 3 peaks in analytical gas chromatography, with retention times identical with those of 1*H*-heptafluoro*cyclo*hexa-1 : 4-diene, 2*H*-heptafluoro*cyclo*hexa-1 : 3-diene, and unchanged starting material, respectively. Separation in the preparative-scale column A (temp. 96°, N_2 flow-rate 9·6 l./hr.) gave the 1*H*-1 : 4-diene (0·61 g.), the 2*H*-1 : 3-diene (b. p. 76°) (0·28 g.), and unchanged 1*H* : 5*H*-*cyclo*hexene (0·24 g.). These three compounds had infrared spectra identical with those of the samples A, C, and D, respectively, described above. The 2*H*-1 : 3-diene was identical also with compound (iii) obtained [1] by dehydrofluorination of 1*H* : 4*H*/2*H*- and 1*H*/2*H* : 4*H*-nonafluoro*cyclo*hexane.

(c) *Fluorination*. The *cyclo*hexene (4·5 g.) was fluorinated by passage through the small static cobaltic fluoride reaction vessel.[4] It was introduced from a micro-burette and carried through (temp. 60—65°) in a stream of nitrogen (flow rate 5 l./hr.). The products were condensed from the nitrogen stream in a trap cooled by solid carbon dioxide. Analytical gas chromatography of the product (4·70 g.) showed 4 peaks with retention times the same as those of the compounds named below. Separation in the preparative-scale column A yielded: (i) dodecafluoro*cyclo*hexane (0·11 g.); (ii) undecafluoro*cyclo*hexane (2·02 g.); (iii) 1*H*/3*H*-decafluoro*cyclo*hexane (1·46 g.); and (iv) 1*H* : 3*H*/-decafluoro*cyclo*hexane (0·60 g.). These compounds had infrared spectra identical with those of authentic specimens.[4]

(d) *Spectroscopy*. The *cyclo*hexene had a –HC=CF– infrared band at 1717 cm.$^{-1}$, and $\geq$C–H bands at 3102, 3067, and 2980 cm.$^{-1}$, but there was no selective ultraviolet absorption between 2400 and 3000 Å.

Characterisation of 4H : 5H/-*Octafluorocyclohexene*.—(a) *Oxidation*. The olefin (3·78 g.; b. p. 99°) was oxidised with potassium permanganate (7·68 g.) in dry acetone (750 c.c.), to give an acidic solid (3·88 g.). Distillation of a portion (0·19 g.) at 160° (bath-temp.)/0·5 mm. on to a cold finger gave the very hygroscopic meso-3H : 4H-*hexafluoroadipic acid* (0·11 g.), m. p. 163—165° (Found: C, 28·3; H, 1·8. $C_6H_4O_4F_6$ requires C, 28·4; H, 1·6%). The acid gave a *dianilinium salt* (60%) (from acetone–chloroform), m. p. 200—201° (Found: C, 48·7; H, 4·0%; equiv., 220. $C_{18}H_{18}O_4N_2F_6$ requires C, 49·1; H, 4·1%; equiv., 220), and a *di*-(S-*benzylthiuronium*) *salt* (71%) (from water), m. p. 228—229° [depressed in admixture with the salt of the (±)-acid] (Found: C, 45·5; H, 4·2; F, 19·2. $C_{22}H_{24}O_4N_4S_2F_6$ requires C, 45·0; H, 4·1; F, 19·4%).

(b) *Fluorination*. The *cyclo*hexene (3·6 g.) was passed through the small static cobaltic fluoride reaction vessel (temp. 50°) in nitrogen (flow-rate 5 l./hr.). The product (2·0 g.) was isolated as previously, and analytical gas chromatography showed that it contained two components. Separation in the preparative-scale column A afforded undecafluoro*cyclo*hexane (0·9 g.) and 1*H* : 2*H*/-decafluoro*cyclo*hexane [3, 17] (0·7 g.). The last compound had the correct infrared spectrum.

(c) *Dehydrofluorination*. The olefin (0·81 g.), potassium hydroxide (4 g.), and water (5 c.c.) were boiled together for 3½ hr. The product was separated, washed with water, and dried ($MgSO_4$). Analytical gas chromatography showed two components with retention times corresponding to those of 1*H*-heptafluoro*cyclo*hexa-1 : 4-diene and hexafluorobenzene. Separation (0·29 g.) by preparative-scale gas chromatography yielded the 1 : 4-diene

[20] Godsell, Stacey, and Tatlow, *Nature*, 1956, **178**, 199.

XUM

(0·18 g.) and hexafluorobenzene [20] (0·05 g.). These two compounds had correct infrared spectra.

(d) *Spectroscopy.* The olefin had an –FC=CF– absorption band at 1750 cm.$^{-1}$ and $\geq$C–H bands at 2979 and 2975 cm.$^{-1}$, the last two characteristic of hydrogen on carbon β to the olefinic group. There was no selective ultraviolet absorption.

Oxidation of meso-3H : 4H-*Hexafluoroadipic Acid.*—The acid (3·30 g.), potassium permanganate (10 g.), potassium hydroxide (10 g.), and water (150 c.c.), refluxed together for 16 hr., yielded difluoromalonic acid (73%).

Attempted Optical Resolution of meso-3H : 4H-*Hexafluoradipic Acid.*—The acid (2·53 g.) in ethanol (25 c.c.) was added to a solution of (−)-brucine (7·85 g.) in ethanol (125 c.c.). The mixture was kept for 10 min. and then evaporated to dryness. The solid (9·89 g.) was twice recrystallised from water, to yield the *dibrucine salt* (30% recovery), m. p. 205—207° (Found: C, 59·4; H, 5·4. $C_{52}H_{56}O_{12}N_4F_6$ requires C, 59·9; H, 5·4%).

Repeated recrystallisation of this salt did not change the optical rotatory power, and specimens of acid isolated from various crops all had m. p. and mixed m. p. 163—164° and were optically inactive. Their infrared spectra were identical with each other, and were different from those [1] of (+)- and (−)-3*H* : 4*H*-hexafluoroadipic acid and their racemate.

Characterisation of 3H : 4H/-*Octafluoro*cyclo*hexene.*—(a) *Oxidation.* The compound (3·22 g.; b. p. 116°) was oxidised with potassium permanganate (6·00 g.) in dry acetone (700 c.c.) and gave an acidic solid (2·86 g.). Distillation of a sample (0·21 g.) at 135° (bath-temp.)/0·1 mm. on to a cold finger gave the very hygroscopic (±)-erythro-2H : 3H-*hexafluoroadipic acid* (0·16 g.), m. p. 107—109° (Found: C, 27·7; H, 1·4%; equiv., 123. $C_6H_4O_4F_6$ requires C, 28·4; H, 1·6%; equiv., 127). The crude acid in ether was treated with aniline to give *dianilinium* 2H : 3H-*hexafluoroadipate* (60% overall), m. p. 169—171° (from acetone–chloroform) (Found: C, 49·1; H, 4·1; F, 25·9. $C_{18}H_{18}O_4N_2F_6$ requires C, 49·1; H, 4·1; F, 25·9%). The dianilinium salt (0·36 g.) in water with *S*-benzylthiuronium chloride gave the *di*-(S-*benzylthiuronium*) *salt* (0·29 g.), m. p. 216—217° (from water) (Found: C, 45·0; H, 4·1; F, 19·5%).

(b) *Fluorination.* The olefin (3·3 g.), fluorinated as before in the small static cobaltic fluoride vessel,[4] yielded a product (2·60 g.), a sample (0·43 g.) of which was separated in the preparative-scale column A (temp. 80°) to give (i) undecafluoro*cyclo*hexane (0·09 g.) and (ii) 1H : 2H/-decafluoro*cyclo*hexane (0·18 g.). These compounds had correct infrared spectra.

(c) *Dehydrofluorination.* The *cyclo*hexene (40·4 g.), potassium hydroxide (41 g.), and water (145 c.c.) were boiled together for 2 hr. The organic layer (containing 29·4 g.) was separated, washed with water, and dried ($MgSO_4$). Examination by analytical gas chromatography showed the presence of 5 components. Separation (27·6 g.) in the preparative-scale column B gave: (i) 1*H*-heptafluoro*cyclo*hexa-1 : 3-diene (4·1 g.); (ii) 2*H*-heptafluoro*cyclo*hexa-1 : 3-diene (9·7 g.); (iii) hexafluorobenzene (0·4 g.); (iv) (suspected) 3*H* : 6*H*-octafluoro*cyclo*hexene (0·1 g.); and (v) unchanged 3*H* : 4*H*/-octafluoro*cyclo*hexene (9·9 g.). Fractions (i), (ii), (iii), and (v) had correct infrared spectra.

(d) *Spectroscopy.* The *cyclo*hexene had a –FC=CF– infrared band at 1746 cm.$^{-1}$ and $\geq$C–H bands at 2979 and 2960 cm.$^{-1}$, characteristic of hydrogen on carbons respectively β and α to the olefinic group. No selective absorption was shown between 2400 and 3000 Å.

Oxidation of (±)-erythro-2H : 3H-*Hexafluoroadipic Acid.*—The acid (0·75 g.) was refluxed with potassium permanganate (2·50 g.), potassium hydroxide (2·50 g.), and water (50 c.c.) for 20 hr., to give tetrafluorosuccinic acid (40%).

Fluorination of 1H : 2H/4H-*Nonafluoro*cyclo*hexane.*—This compound (15·0 g.; b. p. 107°) was introduced from an electrically heated micro-burette into the small static cobaltic fluoride reaction vessel which was at 175—180°. A stream of nitrogen was blown through, and the product (14·0 g.) was washed with water, separated, and dried ($MgSO_4$). Analytical gas chromatography (102°; N_2 flow-rate 1·2 l./hr.) showed the presence of 4 peaks, with retention times the same as those of the compounds mentioned below. Separation (4·43 g.) in the preparative-scale column A gave: (i) undecafluoro*cyclo*hexane (0·03 g.); (ii) a mixture (0·50 g.) of 1*H*/4*H*- and 1*H*/3*H*-decafluoro*cyclo*hexane; [4] (iii) 1*H* : 2*H*/-decafluoro*cyclo*hexane (0·03 g.); and (iv) 1*H* : 2*H*/4*H*-nonafluoro*cyclo*hexane (3·01 g.). The presence of the two compounds in fraction (ii) was shown by gas-phase chromatography on tritolyl phosphate–kieselguhr (1 : 3) (62°; N_2 flow-rate 0·9 l./hr.), and fractions (i)—(iv) had correct infrared spectra.

Fluorination of 1H-*Heptafluoro*cyclo*hexa*-1 : 3-*diene.*—The diene (7·5 g.; b. p. 71·5—72·5°) was introduced into the small static vessel [4] at 55—65° in a nitrogen stream (flow-rate 5 l./hr.).

XUM

The products (7·1 g.) were blown from the vessel by nitrogen, and gas-phase chromatography showed the presence of 7 components. Separation (6·13 g.) in the preparative-scale column A (75°; N_2 flow-rate 9·4 l./hr.), gave (i) a mixture (0·11 g.) of dodecafluoro*cyclo*hexane and decafluoro*cyclo*hexene; (ii), undecafluoro*cyclo*hexane (2·27 g.); (iii) a mixed fraction (0·60 g.) containing compounds (ii) and (iv) only; (iv) 1*H*-nonafluoro*cyclo*hex-1-ene (1·80 g.); (v) 1*H*-heptafluoro*cyclo*hexa-1 : 4-diene (0·16 g.); (vi) 4*H*-nonafluoro*cyclo*hex-1-ene [5] (0·08 g.); and (vii) 3*H*-nonafluoro*cyclo*hex-1-ene [5] (0·21 g.). All fractions had correct infrared spectra.

Fluorination of 2H-*Heptafluoro*cyclo*hexa*-1 : 3-*diene*.—The diene (4·2 g.; b. p. 76°), fluorinated as the 1*H*-isomer, yielded a product (6·2 g.) which on analysis by gas chromatography showed the presence of 6 components. Separation as before yielded: (i) dodecafluoro*cyclo*hexane (0·01 g.); (ii) undecafluoro*cyclo*hexane (3·51 g.); (iii) an intermediate fraction (0·69 g.) containing compounds (ii) and (iv) only; (iv) 1*H*-nonafluoro*cyclo*hexene (0·75 g.); (v) 1*H*-heptafluoro*cyclo*hexa-1 : 4-diene (0·03 g.) contaminated with compound (iv); and (vi) a mixture (0·1 g.) of 4*H*- and 3*H*-nonafluoro*cyclo*hexene. These fractions were identified by their infrared spectra.

Preparation of the Four Isomeric 1H : 2H : 4H-*Nonafluoro*cyclo*hexanes* (*with* J. A. Godsell).—4*H*-Nonafluoro*cyclo*hexene (7·0 g.; b. p. 69°) and an excess of chlorine were sealed together in a " Pyrex " tube which was irradiated with ultraviolet light for 20 hr. The product (7·5 g.) was taken up in ether, washed with sodium metabisulphite solution, then with water, dried ($MgSO_4$), and filtered.

Reduction was carried out in 3 portions. Chlorofluorocarbon (2·5 g.) in ether (30 c.c.) was added slowly to lithium aluminium hydride (0·6 g.) in ether (10 c.c.) at 0° with stirring. After 3½ hr., sulphuric acid was added cautiously, the ethereal layer was separated, and the aqueous layer extracted once with ether. The ether layers and extracts from the three reductions were combined, dried ($MgSO_4$), and filtered. The bulk of the ether was removed by fractional distillation (6″ column packed with 1/16″ × 1/16″ Dixon gauze spirals), and the residue (4·8 g.) was examined by analytical gas chromatography (110°; N_2 flow-rate 1·2 l./hr.), to show the presence of 5 components. The mixture was separated in the preparative-scale column A to give: (i) diethyl ether (2·20 g.); (ii) 1*H* : 4*H*/2*H*-nonafluoro*cyclo*hexane [1] (0·03 g.); (iii) 1*H* : 2*H*/4*H*-nonafluoro*cyclo*hexane (0·46 g.); (iv) 1*H*/2*H* : 4*H*-nonafluoro*cyclo*hexane [1] (0·30 g.); and (v) 1*H* : 2*H* : 4*H*/nonafluoro*cyclo*hexane (0·51 g.) (Found: C, 29·4; H, 1·3%). Compounds (ii)—(v) had correct infrared spectra.

Dehydrofluorination of 1H : 2H : 4H/-*Nonafluoro*cyclo*hexane*.—The compound (13·0 g.; b. p. 124°), potassium hydroxide (50 g.), and water (50 c.c.) were shaken together at 15° for 1¼ hr. The organic layer (8·6 g.) was separated, washed with water, and dried ($MgSO_4$). Analytical gas chromatography (tritolyl phosphate–kieselguhr 1 : 3; 120°; N_2 flow-rate 1·2 l./hr.) showed the presence of 7 components. Separation of part of the mixture (8·50 g.) in the preparative-scale column A afforded: (i) 1*H*-heptafluoro*cyclo*hexa-1 : 4-diene (1·05 g.); (ii) a mixture (0·63 g.) of compound (i) and 1*H*-heptafluoro*cyclo*hexa-1 : 3-diene; (iii) 2*H*-heptafluoro*cyclo*hexa-1 : 3-diene (0·25 g.); (iv) 1*H* : 5*H*-octafluoro*cyclo*hexene (0·93 g.); (v) 1*H* : 4*H*-octafluoro*cyclo*hexene (1·08 g.), b. p. 86°, n_D^{21} 1·3260 (Found: C, 31·9; H, 0·9%), for which were cited,[13] b. p. 87—88°, n_D^{20} 1·320; (vi) 4*H* : 5*H*/-octafluoro*cyclo*hexene (1·53 g.), b. p. 99°; and (vii) 3*H* : 4*H*/-octafluoro*cyclo*hexene (1·38 g.), b. p. 116°. Fractions (i)—(iv), (vi), and (vii) had infrared spectra identical with those of authentic specimens.

Characterisation of 1H : 4H-*Octafluoro*cyclo*hexene*.—(a) *Oxidation*. The compound (b. p. 86°) yielded 3*H*-heptafluoroadipic acid.

(b) *Dehydrofluorination*. The *cyclo*hexene (7·1 g.), potassium hydroxide (8 g.), and water (10 c.c.) were boiled together for 5 hr. The organic layer (6·4 g.) was separated, washed with water, and dried ($MgSO_4$). Analytical gas chromatography (100°; N_2 flow-rate 1·1 l./hr.) gave 3 peaks. Separation (5·0 g.) in the preparative-scale column A (85°; N_2 flow-rate 9·4 l./hr.) gave: (i) 1*H*-heptafluoro*cyclo*hexa-1 : 4-diene (2·0 g.); (ii) 1*H*-heptafluoro*cyclo*hexa-1 : 3-diene (1·2 g.); and (iii) 1*H* : 4*H*-octafluoro*cyclo*hexene (1·1 g.). These compounds had correct infrared spectra. The 1*H*-1 : 3-diene was identical with fraction (ii) obtained [1] by dehydrofluorination of 1*H* : 4*H*/2*H*- and 1*H*/2*H* : 4*H*-nonafluoro*cyclo*hexane.

(c) *Fluorination*. The *cyclo*hexene (7·5 g.) on passage through the small static cobaltic fluoride vessel at 45—55° gave a product (8·0 g.) which on analytical gas chromatography showed the presence of 4 components. The first two peaks were identified chromatographically

as due to dodeca- and undeca-fluoro*cyclo*hexane. Examination on an alternative packing (silicone oil–silicone rubber 1 : 3; 75°; N_2 flow-rate 0·85 l./hr.) resolved the final peak into two components. Separation of a sample (5·80 g.) in the preparative-scale column A (87°; N_2 flow-rate 9·6 l./hr.) afforded: (i) 1*H*/4*H*-decafluoro*cyclo*hexane (1·01 g.); and (ii) a mixture (3·29 g.) of 1*H* : 4*H*/decafluoro*cyclo*hexane and unchanged 1*H* : 4*H*-octafluoro*cyclo*hex-1-ene. The two components emerging first were not collected. The other two fractions were identified by infrared spectra. Infrared-absorption data indicated that fraction (ii) contained approx. equal quantities of 1*H* : 4*H*/-decafluoro*cyclo*hexane (b. p. 86°), and 1*H* : 4*H*-octafluoro*cyclo*hexene (b. p. 86°), but no other compound.

(d) *Spectroscopy*. The *cyclo*hexene had an infrared –HC=CF– absorption band at 1713 cm.$^{-1}$ but no selective absorption over the range 2400—3000 Å.

Fluorination of 1*H* : 2*H* : 4*H*/-*Nonafluoro*cyclo*hexane*.—This compound (7·5 g.; b. p. 124°) was introduced into the small static reaction vessel at 205°. The products (9·8 g.) were blown from it by a stream of nitrogen, and analytical gas chromatography showed the presence of 6 components. Separation of a sample (8·8 g.) in the preparative-scale column A afforded: (i) dodecafluoro*cyclo*hexane (0·01 g.); (ii) undecafluoro*cyclo*hexane (3·1 g.); (iii) 1*H* : 4*H*/-decafluoro*cyclo*hexane (2·1 g.); (iv) 1*H* : 2*H*/-decafluoro*cyclo*hexane (0·5 g.); (v) 1*H* : 3*H*/-decafluoro*cyclo*hexane (0·7 g.); and (vi) unchanged 1*H* : 2*H* : 4*H*/-nonafluoro*cyclo*hexane, b. p. 124°. These compounds had correct infrared spectra.

Fluorination of Benzene by Manganic Fluoride.—Benzene (100 c.c.) was introduced into a vessel, constructed of nickel and of the type described in a previous paper.[21] It was filled with manganic fluoride (3 kg.) and operated at 200—250°. The fluorination was carried out as described for analogous reactions with cobaltic fluoride. The liquid product (170 g.) was removed from the cold trap after the vessel had been swept out with a stream of nitrogen. It was then washed with water, dried ($MgSO_4$), and filtered. The combined products (800 g.) from several runs were fractionally distilled [4′ column packed with Dixon gauze spirals (1/16″ × 1/16″)]. Only two pure fractions were obtained: (i) 1*H* : 4*H*-octafluoro*cyclo*hexene (180 g.), b. p. 86°; and (ii) 1*H* : 2*H* : 4*H*-heptafluoro*cyclo*hexene (80 g.), b. p. 106°. Fear and Thrower obtained [13] an octafluoro-, b. p. 87° (14·7%), and a heptafluoro-*cyclo*hexene-b. p. 106° (8·8%). By infrared spectroscopy, it was shown that fraction (i) was identical with the material of b. p. 86° obtained by dehydrofluorination of 1*H* : 2*H* : 4*H*/-nonafluoro*cyclo*hexane, and that fraction (ii) was identical with the unsaturated component of the fraction, b. p. 106—107°, isolated from the benzene–cobaltic fluoride reaction.

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[21] Barbour, Barlow, and Tatlow, *J. Appl. Chem.*, 1952, **2**, 127.

30. *Fluorocyclohexanes. Part V.** 1H : 4H/2H : 5H-, 1H : 5H/-2H : 4H-, 1H : 2H/4H : 5H-, *and* 1H : 2H : 4H/5H-*Octafluorocyclohexane and Derived Compounds.*

By E. Nield, R. Stephens, and J. C. Tatlow.

Four octafluoro*cyclo*hexanes have been isolated from the products obtained by the fluorination of benzene with cobaltic fluoride. Of these, three give, on dehydrofluorination, the same four unsaturated compounds which have been separated by preparative-scale gas chromatography and identified by oxidation, spectroscopy, etc., as 1*H* : 5*H*- and 1*H* : 4*H*-hexafluoro*cyclo*hexa-1 : 4-diene, pentafluorobenzene, and 1*H*,4*H*/5*H*-heptafluoro*cyclo*hexene. The fourth octafluoro*cyclo*hexane gives, on dehydrofluorination, the same 1 : 4-dienes, pentafluorobenzene, and 1*H*,4*H* : 5*H*/-heptafluoro*cyclo*hexene. A 1*H* : 2*H* : 4*H* : 5*H*-structure was thus indicated for all four octafluoro*cyclo*hexanes, and the stereochemistry of each was determined by further fluorination to give known nona- and deca-fluoro-*cyclo*hexanes.

As described previously,[1-5] the mixture obtained on vapour-phase fluorination of benzene with cobalt trifluoride at about 150° yields a series of polyfluoro*cyclo*hexanes. The residue remaining after removal of the three major nonafluoro*cyclo*hexane fractions,[4,5] *i.e.*, those having b. p. >107°, has now been examined, and four new octafluoro*cyclo*hexanes have been obtained from it. These fluorohydrocarbons (I, b. p. 118°, m. p. 62°; II, b. p. 125°, m. p. 94°; III, b. p. 133°, m. p. 88°; and IV, b. p. 136°, m. p. 30°) have been isolated by fractional distillation controlled by analytical gas chromatography.[6] Two of them (I and IV) were obtained pure directly from the distillation, but the other two required subsequent treatment for purification.

The compound of b. p. 125° (II) was obtained from a liquid fraction of boiling range 120—127°. This was a minor fraction and could not be separated further by distillation. However, it partly crystallised and the solid consisted largely of a mixture of an octafluoro*cyclo*hexane (II) and a small amount of perfluorodi*cyclo*hexyl. The former (II) was isolated pure by the zone-melting technique.[7] A pure specimen of perfluorodi*cyclo*hexyl was obtained from the crude solid mixture by treatment with aqueous potassium hydroxide. Dehydrofluorination of the fluorohydrocarbon (II) (see below) gave liquid unsaturated products from which perfluorodi*cyclo*hexyl crystallised in the cold. This fluorocarbon may arise from the fluorination of diphenyl, formed by the combination of phenyl radicals which could result from an initial removal of hydrogen from benzene by the fluorinating agent. Such intermediate species obviously react mainly to give fluorobenzenes and thence fluoro*cyclo*hexanes. Alternatively, the perfluorodi*cyclo*hexyl could be formed by the combination of partially fluorinated *cyclo*hexyl, *cyclo*hexenyl, or *cyclo*hexadienyl intermediates arising during the fluorination. Dimerisations of this general type occur frequently during reaction with elementary fluorine, particularly in the liquid phase.[8,9] Though they are not usually encountered in processes involving cobaltic fluoride, a similar effect has been noted[10] in the fluorination of benzene with manganic fluoride.

* Part IV, preceding paper, *q.v.* for nomenclature.

[1] Smith and Tatlow, *J.*, 1957, 2505.
[2] Stephens and Tatlow, *Chem. and Ind.*, 1957, 821.
[3] Evans, Godsell, Stephens, Tatlow, and Wiseman, *Tetrahedron*, 1958, **2**, 183.
[4] Godsell, Stacey, and Tatlow, *Tetrahedron*, 1958, **2**, 193.
[5] Stephens, Tatlow, and Wiseman, preceding paper.
[6] Evans and Tatlow, *J.*, 1955, 1184.
[7] Herington, Handley, and Cook, *Chem. and Ind.*, 1956, 292; Parr, *Roy. Inst. Chem., Lectures, Monographs, and Reports*, 1957, No. 3.
[8] Miller, Ehrenfeld, Phelan, Prober, and Reed, *Ind. Eng. Chem.*, 1947, **39**, 401.
[9] Smith, Stacey, Tatlow, Dawson, and Thomas, *J. Appl. Chem.*, 1952, **2**, 97.
[10] Fear and Thrower, *ibid.*, 1955, **5**, 353.

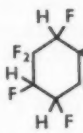
XUM

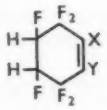
The mother-liquor remaining from the initial crystallisation of the fraction of boiling range 120—127° was shown by analytical gas chromatography to contain six components, and was separated by preparative-scale gas chromatography [11] into five fractions. Four of the compounds present have been characterised. The first component was identified by infrared spectroscopy as perfluorodi*cyclo*hexyl. The second was identical with a hexafluoro*cyclo*hexene to be described in a later paper [12] and was oxidised [13] by potassium permanganate in acetone to give the known [4] (±)-3*H* : 4*H*-hexafluoroadipic acid (V), showing it to be 1*H* : 2*H*,4*H*/5*H*-hexafluoro*cyclo*hexene (VI). The third sub-fraction was a mixture of two saturated hydrofluorocarbons but their identification has been delayed so far by the very small amounts available. The fourth component was identified (see Part IV [5]) as 1*H* : 2*H* : 4*H*/-nonafluoro*cyclo*hexane, b. p. 124°. The fifth sub-fraction was shown by infrared spectroscopy to be 1*H* : 5*H*/2*H* : 4*H*-octafluoro*cyclo*hexane (II).

The fraction of the polyfluoro*cyclo*hexane mixture having b. p. 133° (III) was obtained as a liquid from the distillation but rapidly crystallised, the crystals being freed from liquid impurities by washing with ether. This gave specimens showing no minor peaks in gas chromatography and giving correct analyses for an octafluoro*cyclo*hexane.

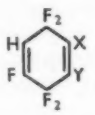
The four octafluoro*cyclo*hexanes (I—IV) were dehydrofluorinated with aqueous potassium hydroxide to give, in each case, a mixture of four compounds, as indicated by gas chromatography. The gas-chromatographic retention times also suggested that the octafluoro*cyclo*hexanes with b. p.s 118° (I), 125° (II), and 136° (IV) each gave the same four products, but that the compound with b. p. 133° (III) gave three products which were the

(I) 1*Ha*:4*He*/2*Ha*:5*He*
(II) 1*Ha*:5*Ha*/2*Ha*:4*Ha*
(III) 1*Ha*:2*He*/4*Ha*:5*He*
(IV) 1*He*:2*Ha*:4*Ha*/5*Ha*

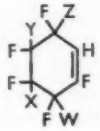




(VI) X=Y=H; 4*H*/5*H*
(VII) X=H, Y=F; 4*H*/5*H*
(VIII) X=H, Y=F; 4*H*:5*H*/



(V)



(IX) X=H, Y=F
(X) X=F, Y=H

	W	X	Y	Z
(XI)	H	F	F	F
(XII)	F	F	F	H
(XIII)	F	F	H	F
(XIV)	F	H	F	F

same as those from the isomers (I, II, and IV), the fourth, that of longest retention time, being different. The compounds were isolated by preparative-scale gas chromatography, and infrared spectroscopy confirmed the above conclusions.

The unsaturated product with the shortest chromatographic retention time had b. p. 71°, and analysed as a hexafluoro*cyclo*hexadiene. On oxidation with potassium permanganate in acetone it gave difluoromalonic acid. There was no strong selective absorption in the range 2400—3000 Å. Two –C=C– absorption bands [14] of roughly similar strengths in the infrared spectrum at 1744 and 1711 cm.$^{-1}$ and a ⩾C–H band [15] at 3082 cm.$^{-1}$ indicated a 1 : 4-diene system with two –CH=CF– groups, and an unsymmetrical arrangement; *i.e.*, the compound was 1*H* : 5*H*-hexafluoro*cyclo*hexa-1 : 4-diene (IX).

This structure was substantiated by fluorination of the diene (IX) with cobaltic fluoride in a small static cylindrical reaction vessel.[3] The liquid product was shown by gas

[11] Evans, Massingham, Stacey, and Tatlow, *Nature*, 1958, **182**, 591.
[12] Nield, Stephens, and Tatlow, unpublished work.
[13] Burdon and Tatlow, *J. Appl. Chem.*, 1958, **8**, 293.
[14] Burdon and Whiffen, *Spectrochim. Acta*, 1958, **12**, 139.
[15] Steele and Whiffen, *Tetrahedron*, 1958, **3**, 181.

chromatography to contain eight components, 1*H*/3*H*- and 1*H* : 3*H*/-decafluoro*cyclo*hexanes being isolated and identified. These two must have arisen by saturation of the double bonds of the diene and established the 1 : 3-disposition of the hydrogen atoms since no isomeric decafluorides were present. A complicating feature of this fluorination, however, was the isolation of 1*H* : 3*H*-octafluoro*cyclo*hexene (XI). The absence of other decafluoro-compounds from the mixture suggested that the 1*H* : 3*H*- arrangement must be preserved in compound (XI). Dehydrofluorination of it afforded the known [4,5] 1*H*- and 2*H*-heptafluoro*cyclo*hexa-1 : 3-dienes, presumably by 1 : 2- and 1 : 4-elimination respectively. Oxidation with potassium permanganate in the presence of sodium hydrogen carbonate gave the known [6,3] 2*H*-heptafluoroadipic acid. There was an infrared absorption band at 1715 cm.$^{-1}$, typical of the group –CH=CF– and ⩾C–H bands at 3100 and 2961 cm.$^{-1}$ characteristic of hydrogen carried respectively on and α to a double bond. The 1*H* : 3*H*- arrangement (XI) is proved by the formation of two conjugated dienes upon dehydrofluorination. The isomeric 1*H* : 6*H*-octafluoro*cyclo*hexene (XII) should give only 2*H*-heptafluoro*cyclo*hexa-1 : 3-diene. This compound (XII) has been prepared [16] in other work; it differs from compound (XI) and in fact does give only the 2*H*-1 : 3-diene with alkali. Compound (XI) must have arisen by selective fluorination of a double bond in a 1*H* : 3*H*-hexafluoro*cyclo*hexa-1 : 3-diene formed by a rearrangement of the diene (IX). Other cases of the migration of double bonds in cyclic 1 : 4- and 1 : 3-dienes are now known [17] and examples of the same type were observed in similar fluorinations described [5] in Part IV. The other five components of the original mixture obtained from the fluorination were those expected from a 1*H* : 5*H*-hexafluoro*cyclo*hexa-1 : 4-diene (IX), *viz.*, perfluoro*cyclo*hexane, undecafluoro*cyclo*hexane, 1*H*-nonafluoro*cyclo*hexene, unchanged diene, and 1*H* : 5*H*-heptafluoro*cyclo*hexene (XIII) which were all identified by infrared spectroscopy.

The second compound from the original dehydrofluorinations of the octafluoro*cyclo*hexanes (I—IV) had b. p. 75° and was shown to be the isomeric 1*H* : 4*H*-hexafluoro*cyclo*hexa-1 : 4-diene (X) by the same methods. Thus, oxidation with potassium permanganate in acetone gave difluoromalonic acid and fluorination with cobalt trifluoride gave a mixture containing six components, identified by infrared spectroscopy and gas chromatography as perfluoro*cyclo*hexane, undecafluoro*cyclo*hexane, 1*H*-nonafluoro*cyclo*hexene, 1*H*/4*H*- and 1*H* : 4*H*/-decafluoro*cyclo*hexane, and 1*H* : 4*H*-octafluoro*cyclo*hexene (XIV). This fluorination was not complicated by migration of the type previously observed since such a change would not produce any additional products. The diene (X) did not show selective absorption in its ultraviolet spectrum over the range 2400—3000 Å. In the infrared spectrum it had a ⩾C–H band at 3087 cm.$^{-1}$ and –C=C– bands at 1707 (very strong) and 1737 cm.$^{-1}$ (weak). Two bands would not be expected for a symmetrical molecule of this type and the effect is considered to arise from the non-planarity of the *cyclo*hexa-1 : 4-diene ring,[14] this being supported by the very unequal intensities of the two bands. Models indicate that a boat form of this diene ring is less strained than a planar one.

The third dehydrofluorination product of the octafluoro*cyclo*hexanes (I—IV) had b. p. 85° and was characterised as pentafluorobenzene in the manner already described.[2] Further reactions of this important aromatic compound are reported in the following paper.

The fourth unsaturated product was obtained from the dehydrofluorinations of three octafluoro*cyclo*hexanes (I, II, and IV) and had b. p. 104°. Its analysis indicated a heptafluoro*cyclo*hexene and it was found to be identical with the 1*H*,4*H*/5*H*-heptafluoro*cyclo*hexene (VII) described earlier.[4] A different heptafluoro*cyclo*hexene (VIII) was obtained from the dehydrofluorination of the octafluoro*cyclo*hexane (III) of b. p. 133°. On oxidation with potassium permanganate in acetone compound (VIII) gave the known [5] *meso*-3*H* : 4*H*-hexafluoroadipic acid (V). There was an infrared absorption band at 1720 cm.$^{-1}$, characteristic of a –CH=CF– group, and a ⩾C–H band at 2980 cm.$^{-1}$ indicating the presence

[16] Evans and Tatlow, unpublished work.
[17] Gething, Patrick, and Tatlow, unpublished work.

of hydrogen on the carbon atoms β to this double bond. Compound (VIII) was thus 1*H*,4*H* : 5*H*/-heptafluoro*cyclo*hexene.

A 1*H* : 2*H* : 4*H* : 5*H*-system was thus indicated for the four octafluoro*cyclo*hexanes described. By eliminations of the normal type, a 1*H* : 2*H* : 3*H* : 4*H*-system on dehydrofluorination could possibly give four stable hexafluoro*cyclo*hexa-1 : 3-dienes but no stable hexafluoro*cyclo*hexa-1 : 4-diene, and a 1*H* : 2*H* : 3*H* : 5*H*-system would give no stable octafluoro*cyclo*hexa-1 : 3- or -1 : 4-diene. The term " stable dienes " here means compounds without >CHF groups. 1 : 3- or 1 : 4-Dienes with >CHF groups are in effect aromatic fluoro-compounds with hydrogen fluoride added to the ring and it is unlikely that they would survive in the relatively drastic dehydrofluorination conditions employed. No intermediates of this type have been found so far in any of the reactions which have given aromatic fluoro-compounds.

The stereochemical structures of the octafluoro*cyclo*hexanes (I—IV) were deduced by further fluorination to the known nona- and deca-fluoro*cyclo*hexanes described earlier.[1-5] The isomer (I) of b. p. 118° gave 1*H*a : 4*H*e/2*H*a-nonafluoro*cyclo*hexane and 1*H*a/2*H*a-, 1*H*a/3*H*e-, and 1*H*a : 4*H*e/-decafluoro*cyclo*hexane, together with undecafluoro*cyclo*hexane and perfluoro*cyclo*hexane. This establishes the stereochemical structure as 1*H*a : 4*H*e/2*H*a : 5*H*e-octafluoro*cyclo*hexane (I). In the same way, the isomer (II) of b. p. 125° gave 1*H*a/2*H*a : 4*H*a-nonafluoro*cyclo*hexane, 1*H*a/2*H*a-, 1*H*a/4*H*a-, and 1*H*a : 3*H*a/-decafluoro-*cyclo*hexane, undecafluoro*cyclo*hexane, and perfluoro*cyclo*hexane. These compounds can arise only from a 1*H*a : 5*H*a/2*H*a : 4*H*a-octafluoro*cyclo*hexane (II). Likewise the isomer of b. p. 133° was shown to be the 1*H*a : 2*H*e/4*H*a : 5*H*e-compound (III) since it gave on further fluorination 1*H*a : 2*H*e/4*H*a-nonafluoro*cyclo*hexane, and 1*H*a/4*H*a-, 1*H*a/3*H*e-, and 1*H*a : 2*H*e/-decafluoro*cyclo*hexane, together with the derived undecafluoro- and perfluoro-*cyclo*hexanes. The fourth octafluoro*cyclo*hexane (IV) of b. p. 136°, on fluorination, gave a mixture of all four 1*H* : 2*H* : 4*H*-nonafluoro*cyclo*hexanes and five of the derived decafluoro*cyclo*hexanes, besides undecafluoro- and perfluoro-*cyclo*hexanes. Hence the parent compound is the 1*H*e : 2*H*a : 4*H*a/5*H*a-octafluoro*cyclo*hexane (IV). The fifth octafluoro-*cyclo*hexane, the 1*H*a : 2*H*e : 4*H*e : 5*H*a/-isomer, which contains the structural features of the three highest-boiling decafluoro*cyclo*hexanes (which are in fact *cis*), is as yet unknown. It is expected to boil at about 150° or above, and should give only the 1*H*e : 2*H*a : 4*H*a/-nonafluoro*cyclo*hexane on further fluorination. Since this nonafluoro-compound is present in the polyfluoro*cyclo*hexane mixture in only small amounts the fifth octafluoro-compound also may well be a minor constituent.

The structural allocations arrived at in this way are in general agreement with the results of the dehydrofluorinations. The octafluoro*cyclo*hexanes of b. p. 133° and 136° lost hydrogen fluoride more readily than did the two isomers of b. p. 118° and 125°. The isomer of b. p. 133° gave a higher proportion of the hexafluoro*cyclo*hexa-1 : 4-dienes and less pentafluorobenzene, as would be expected from its 1*H*a : 2*H*e/4*H*a : 5*H*e-system which should undergo *trans*-eliminations [1,5] in the –CHF–CHF– groupings with comparative ease. Likewise, the 1*H* : 2*H* : 4*H*/5*H*-isomer was dehydrofluorinated at room temperature to give almost exclusively the 1*H*,4*H*/5*H*-heptafluoro*cyclo*hexene (VII) by an internal *trans*-elimination in the *cis*-CHF–CHF-system. Further dehydrofluorination of this olefin was, however, much more difficult. Further proof that the 4*H*/5*H*-arrangement in this *cyclo*hexene (VII) is *trans* was provided [4] by oxidation to the hexafluoroadipic acid (V), which gives a resolvable brucine salt. On the other hand, the existence of two *cis*-arrangements in the 1*H*a : 2*H*e/4*H*a : 5*H*e-isomer, b. p. 133° (III), was supported by oxidation of the derived 1*H*,4*H* : 5*H*/-heptafluoro*cyclo*hexene (VIII) to the unresolvable [5] *meso*-3*H* : 4*H*-hexafluoroadipic acid (V).

The relatively rapid formation of pentafluorobenzene on dehydrofluorination of the 1*H* : 4*H*/2*H* : 5*H*-isomer (I) and the comparative difficulty of dehydrofluorinating the 1*H*,4*H*/5*H*-heptafluoro*cyclo*hexene (VII) indicate that some simultaneous elimination of hydrogen fluoride occurs, and that this *cyclo*hexene is not an intermediate for all of the aromatic compound formed.

XUM

Experimental

Techniques.—Oxidations, gas chromatography, and infrared measurements were carried out as before,[5] unless otherwise stated.

1H : 4H/2H : 5H-, 1H : 5H/2H : 4H-, 1H : 2H/4H : 5H-, and 1H : 2H : 4H/5H-*Octafluoro*cyclo*hexane.*—Fractional distillation controlled by analytical gas chromatography of the partly fluorinated *cyclo*hexane mixture [5] having b. p. >107° gave the following fractions:

Fraction (*A*). This was 1H : 4H/2H : 5H-*octafluoro*cyclo*hexane*, m. p. 60—62°, b. p. 117—118°. It gave a single peak (No. 11 in the table of results given earlier [1]) in analytical gas chromatography (Found: C, 31·3; H, 1·8. $C_6H_4F_8$ requires C, 31·6; H, 1·8%). The yield was approximately 5—10% of the original mixture with a cobaltic fluoride reaction vessel at about 150°; this yield may be increased by using a lower temperature.

Fraction (*B*). This had boiling range 120—127° (*ca.* 0·5% of the original mixture) and was initially a liquid at 15°, but on being kept deposited a highly crystalline solid (i) which was removed by filtration from the mother-liquor (ii). The solid (i) had m. p. 86—88° but was impure. Application of the zone-melting technique [7] [tube, 9″ × 0·25″ (internal diameter); 20 passes of heated zone at tube movement of 3″/hr.] afforded, as a top zone, 1H : 5H/2H : 4H-*octafluoro*cyclo*hexane*, m. p. 93—94°, b. p. 125° (Found: C, 31·8; H, 2·1%). The yield was about 0·2% of the original polyfluoride mixture.

The main impurity in the original deposit (i) was perfluorodi*cyclo*hexyl which was isolated after dehydrofluorination of the crude octafluoride (see below).

The mother-liquor (ii) (7·8 g.) was separated into its constituents by preparative-scale gas chromatography (column A) to give: (*a*) a small amount of perfluorodi*cyclo*hexyl; (*b*) 1*H* : 2*H*, 4*H*/5*H*-hexafluoro*cyclo*hexene (1·4 g.); (*c*) a mixed fraction (0·3 g.); (*d*) 1*H* : 2*H* : 4*H*/-nonafluoro*cyclo*hexane (2·7 g.), b. p. 124°; (*e*) 1*H* : 5*H*/2*H* : 4*H*-octafluoro*cyclo*hexane (1·4 g.), b. p. 125°. Perfluorodi*cyclo*hexyl was identified by its infrared spectrum which was identical with that of an authentic specimen.[18] Sub-fraction (*b*) was characterised by oxidation and by the identity of its infrared spectrum with that of material obtained from another source.[12] Sub-fraction (*c*) was a mixture of two saturated compounds but the very small amount available has prevented identification. Sub-fraction (*d*) was identified as described in Part IV.[5] Sub-fraction (*e*) was identified as the octafluoro*cyclo*hexane of b. p. 125°, by infrared spectroscopy.

Fraction (*C*). This had b. p. 133° but rapidly crystallised, and was then washed with a small amount of diethyl ether. It was 1H : 2H/4H : 5H-*octafluoro*cyclo*hexane*, m. p. 86—88° (Found: C, 31·2; H, 1·6%). The yield was approximately 0·2% of the partially fluorinated mixture.

Fraction (*D*). This was 1H : 2H : 4H/5H-*octafluoro*cyclo*hexane*, b. p. 136°, m. p. 30° (Found: C, 31·5; H, 1·7%), and constituted approx. 5—10% of the partially fluorinated *cyclo*hexane mixture.

The intermediate fractions having boiling ranges 107—117°, 118—120°, 127—133°, and 133—136° contained no other compounds.

Dehydrofluorination of 1H : 4H/2H : 5H-*Octafluoro*cyclo*hexane.*—The octafluoro*cyclo*hexane (34·0 g.; b. p. 118°), potassium hydroxide (60·0 g.), and water (60 c.c.) were heated together under reflux for 4½ hr. with stirring. The organic phase (21·3 g.) was separated, washed with water, and dried ($MgSO_4$). Analytical gas chromatography (105°; N_2 flow-rate 1·0 l./hr.) revealed four peaks. A typical separation of the mixture (4·0 g.) in the preparative-scale gas chromatography column A gave: (i) a mixture (0·4 g.) of 1*H* : 5*H*- and 1*H* : 4*H*-hexafluoro*cyclo*hexa-1 : 4-dienes; (ii) *pentafluorobenzene* (2·6 g.), b. p. 85°, n_D^{18} 1·3931 (Found: C, 42·8; H, 0·7; F, 57·1. C_6HF_5 requires C, 42·9; H, 0·7; F, 56·5%); and (iii) 1*H*,4*H*/5*H*-heptafluoro*cyclo*hexene (0·7 g.), b. p. 104°, n_D^{19} 1·3420 (Found: C, 34·9; H, 1·3. Calc. for $C_6H_3F_7$: C, 34·6; H, 1·45%), which had an infrared spectrum identical with that of the compound described by Godsell, Stacey, and Tatlow.[4]

The mixture of hexafluoro*cyclo*hexa-1 : 4-dienes (2·03 g.) was separated by further preparative-scale gas chromatography (76°; N_2 flow-rate 9·0 l./hr.) into 1H : 5H-*hexafluoro*cyclo*hexa*-1 : 4-*diene* (1·08 g.), b. p. 71°, n_D^{20} 1·3391 (Found: C, 38·1; H, 1·2; F, 60·3. $C_6H_2F_6$ requires C, 38·3; H, 1·1; F, 60·6%), and 1H : 4H-*hexafluoro*cyclo*hexa*-1 : 4-*diene* (0·33 g.), b. p. 75°, n_D^{17} 1·3419 (Found: C, 38·2; H, 1·2%).

Characterisation of 1H : 5H-*Hexafluoro*cyclo*hexa*-1 : 4-*diene.*—(a) *Oxidation.* The diene

[18] Barbour, Barlow, and Tatlow, *J. Appl. Chem.*, 1952, **2**, 127.

XUM

(0·96 g.; b. p. 71°), potassium permanganate (1·8 g.), and dry acetone (300 c.c.) gave difluoromalonic acid (60%).

(b) *Fluorination.* The diene (6·0 g.), diluted with nitrogen (4—6 l./hr.), was passed during ½ hr. over cobaltic fluoride at 75—80° in the vessel described before.[3] Gas chromatography of the liquid product (4·1 g.) revealed eight components, which were separated by preparative-scale gas chromatography (column A; 86°; N_2 flow-rate 10 l./hr.), which gave a trace of perfluoro*cyclo*hexane, followed by undecafluoro*cyclo*hexane, 1*H*-nonafluoro*cyclo*hexene, and starting material, 1*H*/3*H*-decafluoro*cyclo*hexane (1·5 g.), 1*H* : 5*H*-octafluoro*cyclo*hexene (0·1 g.), 1H : 3H-*octafluoro*cyclo*hexene* (0·26 g.), n_D^{19} 1·3223 (Found: C, 31·6; H, 0·8. $C_6H_2F_8$ requires C, 31·9; H, 0·9%), and 1*H* : 3*H*/-decafluoro*cyclo*hexane (0·24 g.). All but the 1*H* : 3*H*-*cyclo*hexene were identified by their infrared spectra and their gas-chromatographic retention times.

(c) *Spectroscopy.* The diene showed two infrared bands of appreciable strength, at 1744 and 1711 cm.$^{-1}$, suggesting [14] two –CH=CF– groups in a 1 : 4-system. A $\geqslant$C–H band at 3082 cm.$^{-1}$ is typical [15] of olefinic hydrogen. There was no selective absorption in the range 2400—3000 Å.

Characterisation of 1H : 3H-*Octafluoro*cyclo*hexene.*—(a) *Dehydrofluorination.* The octafluoro*cyclo*hexene (0·2 g.), potassium hydroxide (4·0 g.), and water (2 c.c.) were shaken together at 15° for 1 hr. The organic phase was distilled out *in vacuo*, then redistilled *in vacuo* from phosphoric oxide, and the product (0·1 g.) was shown by gas chromatography to contain two components in addition to a very small amount of the unchanged *cyclo*hexene. The infrared absorption spectrum of the mixture established that the compounds were 1*H*- and 2*H*-heptafluoro*cyclo*hexa-1 : 3-diene.[4,5] The relative peak strengths of the two isomers indicated the presence of about three times as much of the 1*H*- as of the 2*H*-isomer. The gas-chromatographic retention times and peak areas were in agreement with these results.

(b) *Oxidation.* The octafluoro*cyclo*hexene (0·4 g.), potassium permanganate (0·7 g.), sodium hydrogen carbonate (1·5 g.), and water (50 c.c.) were shaken together at 15° for 40 hr. The solution was then decolorised by sulphur dioxide, acidified by concentrated sulphuric acid (5 c.c.), and extracted continuously with ether. The ethereal extract was dried ($MgSO_4$), filtered, and evaporated, to leave the crude 2*H*-heptafluoroadipic acid (0·3 g.). The dianilinium salt was prepared in the usual way [6,3] and had m. p. 170° (from acetone–chloroform) (Found: C, 47·2; H, 3·8. Calc. for $C_{19}H_{17}O_4N_2F_7$: C, 47·2; H, 3·7%). From the anilinium salt, di-(*S*-benzylthiuronium) 2*H*-heptafluoroadipate was prepared. After recrystallisation from water it had m. p. 228° (depressed on admixture with the 3*H*-isomer) (Found: C, 43·5; H, 3·8. Calc. for $C_{23}H_{23}O_4N_4S_2F_7$: C, 43·7; H, 3·8%) (lit.,[3] m. p. 169—170° and 232—233°, respectively).

(c) *Spectroscopy.* The *cyclo*hexene showed an infrared absorption band at 1715 cm.$^{-1}$, typical of the grouping –CH=CF–, and $\geqslant$C–H bands at 3100 and 2961 cm.$^{-1}$ characteristic of hydrogen located respectively on a double bond and on an α-carbon atom.

Characterisation of 1H : 4H-*Hexafluoro*cyclo*hexa*-1 : 4-*diene.*—(a) *Oxidation.* The diene (1·0 g.), potassium permanganate (3·2 g.), and dry acetone (300 c.c.) gave difluoromalonic acid (55%).

(b) *Fluorination.* The diene (4·1 g.) diluted with nitrogen (4—6 l./hr.) was passed during 20 min. over cobaltic fluoride at 65—70° in the way described previously. Gas chromatography of the liquid product (2·3 g.) revealed five components which were separated by preparative-scale gas chromatography (column A; 110°; N_2 flow-rate 8·8 l./hr.) into perfluoro*cyclo*hexane (trace), undecafluoro*cyclo*hexane (trace), 1*H*-nonafluoro*cyclo*hexene (trace), 1*H*/4*H*-decafluoro-*cyclo*hexane (0·8 g.), and a mixture (0·6 g.) of 1*H* : 4*H*/-decafluoro*cyclo*hexane and 1*H* : 4*H*/-octafluoro*cyclo*hexene. These compounds were identified by their infrared spectra and by identity of gas-chromatographic retention times.

(c) *Spectroscopy.* The diene showed two bands, typical of two –CH=CF– groups arranged 1 : 4, at 1707 and 1737 cm.$^{-1}$, the latter being appreciably the weaker. There was a $\geqslant$C–H band at 3087 typical of olefinic hydrogen. No selective absorption was shown over the range 2400—3000 Å.

Dehydrofluorination of 1H : 5H/2H : 4H-*Octafluoro*cyclo*hexane.*—The crude octafluoro*cyclo*hexane [50·0 g.; m. p. 86—88°; fraction B (i) above], potassium hydroxide (100 g.), and water (100 c.c.) were heated together under reflux for 18 hr. The organic phase (30·0 g.) was separated whilst still warm and was washed with water. When cooled it deposited crystals (5·4 g.) which were filtered off. These were perfluoro*dicyclo*hexyl, and after recrystallisation from light petroleum (b. p. 80—100°) had m. p. 77—78° (Found: C, 25·1; F, 74·9. Calc. for $C_{12}F_{22}$: C, 25·6;

XUM

F, 74·4%). The infrared absorption spectrum was identical with that of an authentic specimen, prepared [18] by fluorination of diphenyl at 350°.

The liquid product was dried ($MgSO_4$) and shown by gas chromatography to contain four components with retention times identical with those of the four products isolated from the octafluoro*cyclo*hexane of b. p. 118°. Separation (4·5 g.) gave a mixture of 1*H* : 5*H*- and 1*H* : 4*H*-hexafluoro*cyclo*hexa-1 : 4-diene (0·45 g.), pentafluorobenzene (1·8 g.), and 1*H*,4*H*/5*H*-heptafluoro*cyclo*hexene (1·2 g.), all having correct infrared spectra.

The pure octafluoro*cyclo*hexane (8·0 g.; b. p. 125°; m. p. 93—94°), potassium hydroxide (16 g.), and water (16 c.c.) were stirred mechanically and refluxed for 2 hr. Isolation and identification as before afforded only mixed dienes (0·3 g.), pentafluorobenzene (2·1 g.), and 1*H*,4*H*/5*H*-heptafluoro*cyclo*hexene (0·9 g.).

Dehydrofluorination of 1H : 2H/4H : 5H-*Octafluoro*cyclo*hexane*.—The octafluoro*cyclo*hexane (8·0 g.; b. p. 133°), potassium hydroxide (16·0 g.), and water (16 c.c.) were shaken vigorously at 15° for 24 hr. The organic phase (4·9 g.) was separated, washed with water, and dried ($MgSO_4$). Analytical gas chromatography revealed four components. Separation by preparative-scale gas chromatography (column A; 110°; N_2 flow-rate 7·0 l./hr.) gave: (i) 1*H* : 5*H*-hexafluoro*cyclo*hexa-1 : 4-diene (1·7 g.); (ii) 1*H* : 4*H*-hexafluoro*cyclo*hexa-1 : 4-diene (0·8 g.); (iii) pentafluorobenzene (0·3 g.); and (iv) 1H,4H : 5H/-*heptafluoro*cyclo*hexene* (1·35 g.), n_D^{23} 1·3430 (Found: C, 34·7; H, 1·5%). The first three fractions were identified by comparison of chromatographic retention times and infrared spectra with those of authentic specimens.

Characterisation of 1H,4H : 5H/-*Heptafluoro*cyclo*hexene*.—(a) *Oxidation*. The monoene (0·3 g.) was oxidised with potassium permanganate (0·8 g.) in dry acetone (100 c.c.) as described previously. Isolation as usual gave dianilinium *meso*-3*H* : 4*H*-hexafluoroadipate (0·6 g.) which after recrystallisation from acetone–chloroform had m. p. 201—202° (Found: C, 49·0; H, 4·0. Calc. for $C_{18}H_{18}O_4N_2F_6$: C, 49·1; H, 4·1%). This (0·20 g.) gave di-(*S*-benzylthiuronium) *meso*-3*H* : 4*H*-hexafluoroadipate (0·25 g.), m. p. 228—229° undepressed on admixture with a sample [5] of the salt of the *meso*-acid but depressed on admixture with one [4] of the racemic acid (Found: C, 45·0; H, 4·0. Calc. for $C_{22}H_{24}O_4N_4S_2F_6$: C, 45·0; H, 4·1%) (lit.,[5] m. p. 200—201° and 228—229°, respectively).

(b) *Spectroscopy*. The *cyclo*hexene showed an infrared absorption band at 1720 cm.$^{-1}$, typical of the group –CH=CF–, and $\geqslant$C–H bands at 2982 and 3087 cm.$^{-1}$ typical of hydrogen placed respectively β to the double bond and on it.

Dehydrofluorination of 1H : 2H : 4H/5H-*Octafluoro*cyclo*hexane*.—The octafluoro*cyclo*hexane (30·0 g.; b. p. 136°), potassium hydroxide (60 g.), and water (60 c.c.) were shaken together at room temperature for 7 hr. The organic phase (23·7 g.) was separated, washed with water, and dried ($MgSO_4$). Analytical gas chromatography revealed the same four compounds as were obtained from the isomers of b. p. 118° and 125°, but the two dienes and pentafluorobenzene were present in traces only. By preparative-scale gas chromatography (column B), 1*H*,4*H*/5*H*-heptafluoro*cyclo*hexene (18·0 g.), b. p. 104°, n_D^{20} 1·3420, was isolated.

The octafluoro*cyclo*hexane (10·0 g.; b. p. 136°), potassium hydroxide (40 g.), and water (40 c.c.) were kept at 100° for 2 hr. with continuous stirring. The organic phase (4·1 g.) was shown to contain 1*H* : 5*H*- and 1*H* : 4*H*-hexafluoro*cyclo*hexa-1 : 4-diene (11% and 3%, respectively), pentafluorobenzene (44%), and 1*H*,4*H*/5*H*-heptafluoro*cyclo*hexene (42%).

Fluorination of 1H : 4H/2H : 5H-*Octafluoro*cyclo*hexane*.—The octafluoro*cyclo*hexane (7·5 g.; b. p. 118°) was passed during 25 min. over cobaltic fluoride at about 150° in the vessel described before.[3] Gas chromatography of the waxy product (7·8 g.) (after the addition of sufficient ether to a small portion to give a liquid sample) revealed seven components with retention times identical with those of perfluoro*cyclo*hexane, undecafluoro*cyclo*hexane, 1*H*/2*H*-decafluoro*cyclo*hexane, 1*H*/3*H*-decafluoro*cyclo*hexane, 1*H* : 4*H*/-decafluoro*cyclo*hexane, 1*H* : 4*H*/2*H*-nonafluoro*cyclo*hexane, and unchanged 1*H* : 4*H*/2*H* : 5*H*-octafluoro*cyclo*hexane, as established by enrichment of the fluorination mixture with authentic samples [3,4] of these compounds. The nonafluoro-compound and unchanged octafluoride were separated from the mixture by preparative-scale gas chromatography (column A) and identified by their infrared spectra.

Fluorination of 1H : 5H/2H : 4H-*Octafluoro*cyclo*hexane*.—The octafluoro*cyclo*hexane (8·0 g.; b. p. 125°) was passed during 20 min. over cobaltic fluoride at about 170°. Gas chromatography of the waxy product (5·7 g.) revealed six components with retention times the same as those of the compounds mentioned below. The mixture (5·0 g.) was separated by preparative-scale gas chromatography (N_2 flow-rate 9 l./hr.) to give: (i) a mixture (0·4 g.) of perfluoro*cyclo*hexane and

undecafluoro*cyclo*hexane; (ii) 1*H*/2*H*-decafluoro*cyclo*hexane (0·25 g.); (iii) 1*H*/4*H*-decafluoro*cyclo*hexane (1·0 g.); (iv) 1*H* : 3*H*/-decafluoro*cyclo*hexane (0·2 g.); and (v) 1*H*/2*H* : 4*H*-nonafluoro*cyclo*hexane (0·85 g.). All these structures were verified by infrared spectroscopy.

Fluorination of 1H : 2H/4H : 5H-*Octafluoro*cyclo*hexane.*—The octafluoro*cyclo*hexane (8·0 g.; b. p. 133°) was passed during 20 min. over cobaltic fluoride at 160°. Gas chromatography of the waxy product (8·0 g.) revealed five components with retention times the same as those of compounds mentioned below. The mixture (5·0 g.) was separated by preparative-scale gas chromatography (column A; 110°, N_2 flow-rate 9 l./hr.), to give: (i) traces of perfluoro*cyclo*hexane and undecafluoro*cyclo*hexane; (ii) a mixture (2·1 g.) of 1*H*/4*H*- and 1*H*/3*H*-decafluoro*cyclo*hexane; (iii) 1*H* : 2*H*/-decafluoro*cyclo*hexane (trace); and (iv) 1*H* : 2*H*/4*H*-nonafluoro*cyclo*hexane (0·8 g.). Fractions (ii) and (iv) were identified by their infrared spectra.

Fluorination of 1H : 2H : 4H/5H-*Octafluoro*cyclo*hexane.*—The octafluoro*cyclo*hexane (7·5 g.; b. p. 136°) was passed during 20 min. over cobaltic fluoride at 160°. Gas chromatography of the waxy product (8·0 g.) (tritolyl phosphate–kieselguhr 1 : 3; 136°; N_2 flow-rate 0·9 l./hr.) revealed eleven components. The mixture (5·0 g.) was separated by preparative-scale gas chromatography (column A; 106°; N_2 flow-rate 8·6 l./hr.), to give: (i) a mixture (0·2 g.) of perfluoro*cyclo*hexane and undecafluoro*cyclo*hexane; (ii) 1*H*/2*H*-decafluoro*cyclo*hexane (trace); (iii) a mixture (0·5 g.) of 1*H*/4*H*- and 1*H*/3*H*-decafluoro*cyclo*hexane; (iv) 1*H* : 4*H*/-decafluoro*cyclo*hexane (0·1 g.); (v) 1*H* : 4*H*/2*H*-nonafluoro*cyclo*hexane (0·5 g.); (vi) 1*H* : 3*H*/-decafluoro*cyclo*hexane (0·1 g.); (vii) 1*H* : 2*H*/4*H*-nonafluoro*cyclo*hexane (0·7 g.); (viii) 1*H*/2*H* : 4*H*-nonafluoro*cyclo*hexane (0·35 g.); (ix) 1*H* : 2*H* : 4*H*/-nonafluoro*cyclo*hexane (trace); and (x) starting material (1·1 g.). Fractions (iii), (v), (vi), (vii), and (viii) had correct infrared spectra.

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31. *Aromatic Polyfluoro-compounds. Part I. The Synthesis of Aromatic Polyfluoro-compounds from Pentafluorobenzene.*

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Pentafluorobenzene has been prepared by dehydrofluorination of 1*H* : 4*H*/2*H* : 5*H*-, 1*H* : 5*H*/2*H* : 4*H*-, 1*H* : 2*H*/4*H* : 5*H*-, and 1*H* : 2*H* : 4*H*/5*H*-octafluoro*cyclo*hexane. Three general types of reaction are undergone by this new compound: addition to the unsaturated ring system (for example, of chlorine), attack on the fluorine atoms by nucleophilic reagents (*e.g.*, sodium methoxide), and replacement of the hydrogen atom by electrophilic reagents. Fuming sulphuric acid gave pentafluorobenzenesulphonic acid; bromine or iodine in sulphuric acid gave respectively bromopentafluoro- or pentafluoroiodo-benzene. From these a general route to pentafluorophenyl derivatives has been provided since they give, fairly readily, Grignard reagents which react normally, *e.g.*, to give 1-(pentafluorophenyl)ethanol. The bromo-compound also gave decafluorodiphenyl by an Ullmann reaction.

SOME aromatic fluoro-compounds have been known for a considerable time and fluorobenzene derivatives were amongst the first organic fluoro-compounds to be investigated systematically. Aromatic fluoro-compounds have usually been prepared by the Balz–Schiemann reaction,[1] *i.e.*, thermal decomposition of diazonium fluoroborates, most of which are insoluble in water. In this way, *o*-, *m*-, and *p*-difluorobenzene,[2] 1 : 2 : 4-[3] and

[1] Balz and Schiemann, *Ber.*, 1927, **60**, 1186; Booth and Martin, "Boron Trifluoride and its Derivatives," John Wiley and Sons, 1949; Roe, *Organic Reactions*, 1949, **5**, 193.
[2] Schiemann and Pillarsky, *Ber.*, 1929, **62**, 3035.
[3] Schiemann, *J. prakt. Chem.*, 1934, **140**, 97.

XUM

1 : 3 : 5-trifluorobenzene,[4] and 1 : 2 : 4 : 5-[5] and 1 : 2 : 3 : 5-tetrafluorobenzene [6] have been synthesised, the last by stepwise nitration, reduction, diazotisation, and fluorination. However, extension of this method to give pentafluorobenzene broke down owing to the expulsion of two *para*-fluorine atoms, to give 2 : 5-difluorobenzoquinone, during the attempted nitration of the tetrafluorobenzene.[5]

Though pentafluorobenzene was unknown until the present work, hexafluorobenzene, the simplest fluorocarbon of the aromatic series, had been prepared by three methods. First, a small yield was obtained from hexachlorobenzene by saturation of the ring with fluorine and then dehalogenation.[7] A novel method, involving pyrolysis of tribromofluoromethane, was reported recently [8] and under optimum conditions good yields can be obtained;[9] the formation of bromopentafluorobenzene in small yield in this pyrolysis was mentioned but no constants were given. The third method was developed in this Department [10] and consists of dehydrofluorination with aqueous alkali of two nonafluoro*cyclo*hexanes [11] obtained from the partial fluorination of benzene with cobaltic fluoride. It has been extended [12] to the preparation of the hitherto unknown pentafluorobenzene from four octafluoro*cyclo*hexanes [13] isolated later from the same polyfluoro*cyclo*hexane mixture. Pentafluorobenzene has been prepared [11] also by dehydrofluorination of 1*H*,4*H*/5*H*-heptafluoro*cyclo*hexene which was obtained from 4*H*/5*H*-octafluoro*cyclo*hexene (a dehydrofluorination product of the nonafluoro*cyclo*hexanes) by reaction with lithium aluminium hydride in diethyl ether.

The dehydrofluorination of the four octafluoro*cyclo*hexanes [13] obtained from the product of partial fluorination of benzene gave reasonable yields of pentafluorobenzene in three cases. Preparative-scale gas chromatography was used for separation of the aromatic from the other dehydrofluorination products in the early work, but 300 g. or more of the mixtures can be separated efficiently by fractional distillation controlled by analytical gas chromatography.

A detailed study of the general chemistry of both hexafluoro- and pentafluoro-benzene is now in progress in this Department. The former undergoes nucleophilic attack without difficulty, giving pentafluoroaniline [14] with sodamide and pentafluoroanisole [10,15] with methoxide ion, the anisole being attacked in turn by methoxide ion to give a dimethoxy-derivative. Recently,[15] pyridine has been suggested as a useful solvent in which to carry out these reactions. It has of course been observed before that, when negative groups are present, aromatic fluorine is susceptible to nucleophilic attack, *e.g.*, notably in 2 : 4-fluorodinitrobenzene,[16] and another example [17] is the replacement of fluorine already present in the nucleus of an aryldiazonium fluoroborate by chloride ions present in the salt as impurity.

With pentafluorobenzene the effect has been demonstrated in the reaction with sodium methoxide in methanol. A tetrafluoroanisole was obtained in good yield, and analytical gas chromatography indicated the presence of one isomer only, though the orientation has not yet been completed. The reactions of hexa- and penta-fluorobenzene with negative ions show that the fluorine substituents do not impair the aromatic character of the ring. The reactions of such ions with perfluoro-olefins and -diolefins are qualitatively faster and

[4] Finger, Reed, and Finerty, *J. Amer. Chem. Soc.*, 1951, **73**, 153.
[5] Finger, Reed, Burness, Fort, and Blough, *ibid.*, p. 145.
[6] Finger, Reed, and Oesterling, *ibid.*, p. 152.
[7] McBee, Lindgren, and Ligett, *Ind. Eng. Chem.*, 1947, **39**, 378.
[8] Désirant, *Bull. Classe Sci. Acad. roy. Belg.*, 1955, **41**, 759.
[9] Hellmann, Peters, Pummer, and Wall, *J. Amer. Chem. Soc.*, 1957, **79**, 5654.
[10] Godsell, Stacey, and Tatlow, *Nature*, 1956, **178**, 199.
[11] *Idem*, *Tetrahedron*, 1958, **2**, 193.
[12] Stephens and Tatlow, *Chem. and Ind.*, 1957, 821.
[13] Nield, Stephens, and Tatlow, preceding paper.
[14] Forbes, Richardson, and Tatlow, *Chem. and Ind.*, 1958, 630.
[15] Pummer and Wall, *Science*, 1958, **127**, 643.
[16] Sanger, *Biochem. J.*, 1945, **39**, 507.
[17] Finger and Oesterling, *J. Amer. Chem. Soc.*, 1956, **78**, 2593.

often take the form of progressive addition–elimination stages. However, addition to the unsaturated ring of pentafluorobenzene can be accomplished under different conditions. As with hexafluorobenzene,[10] addition of chlorine was promoted by ultraviolet irradiation, presumably owing to a radical process. The product was a hexachloropentafluoro*cyclo*hexane, saturation of the ring being completed before replacement of the hydrogen under these conditions.

The usual type of aromatic substitution, that of electrophilic replacement of the hydrogen atom, has also been studied with pentafluorobenzene. It is of considerable value since it has provided the route to several new pentafluorophenyl derivatives and thus opened the way to a study of the effect of this strongly electron-attracting system on various functional groups.

Sulphonation with oleum (20% sulphur trioxide) or with stabilised sulphur trioxide at room temperature readily gave a high yield of the hygroscopic, crystalline pentafluorobenzenesulphonic acid, which was characterised as the anilinium and the *S*-benzylthiuronium salt. It was of interest to observe evidence of slight surface activity in the sodium salt. Unfortunately, the susceptibility of the nuclear fluorine atoms to attack by anions rendered the acid of little apparent use for the preparation of other substituted pentafluorobenzenes. Thus, when a dry finely divided mixture of sodium cyanide and sodium pentafluorobenzenesulphonate was heated to about 80° a violent reaction occurred, with evolution of a large volume of gas, to leave a carbonaceous residue. Possibly substitution of cyanide for fluorine occurred and the highly cyanogenated sulphonic acid then decomposed with the evolution of nitrogen.

Application to pentafluorobenzene of the bromination conditions successfully employed earlier[18] for the preparation of *p*-dibromotetrafluorobenzene from 1 : 2 : 4 : 5-tetrafluorobenzene (bromine in the presence of oleum) gave a good yield of bromopentafluorobenzene. Likewise with iodine and oleum pentafluoroiodobenzene was obtained. When heated with copper bronze in a sealed tube pentafluorobromobenzene underwent a classical Ullmann reaction and gave in excellent yield the new aromatic fluorocarbon, decafluorodiphenyl. Both the bromo- and the iodo-compound reacted fairly easily with magnesium in dry ether, to produce the corresponding Grignard reagent. The reactions did not seem to be so difficult and the reagents were apparently more stable than in the perfluoroalkyl series,[19] nor was the use of very pure magnesium necessary. Pentafluorophenylmagnesium bromide underwent several typical reactions. With water, pentafluorobenzene was regenerated, and analogously, with deuterium oxide, deuteropentafluorobenzene was prepared for spectroscopic purposes, material of high purity being obtained. However, reaction of the iodo-Grignard reagent with carbon dioxide gave a very poor yield of the known pentafluorobenzoic acid.[20] With acetaldehyde, a smooth reaction occurred to give 1-(pentafluorophenyl)ethanol, characterised as its 3 : 5-dinitrobenzoate. This alcohol with phosphoric oxide gave pentafluorophenylethylene, characterised as its dibromo-addition compound and readily polymerised by benzoyl peroxide or ultraviolet irradiation. Attempts to hydrate the double bond of pentafluorostyrene in sulphuric acid were unsuccessful: under mild conditions no reaction occurred, and more drastic ones led to polymer formation. The styrene was oxidised[21] by permanganate in acetone to pentafluorobenzoic acid, characterised as its *S*-benzylthiuronium salt.

Attempted preparations of pentafluorobenzaldehyde from the Grignard reagent by reaction with ethyl orthoformate or 3 : 4-dihydro-6-methyl-3-*p*-tolylquinazoline methiodide[22] gave rather poor yields. The sodium bisulphite compound was, therefore, prepared directly to facilitate purification and was subsequently decomposed with dilute sulphuric acid to regenerate the slightly water-soluble aldehyde. This was identified as its

[18] Hellmann and Bilbo, *J. Amer. Chem. Soc.*, 1953, **75**, 4590.
[19] Henne and Francis, *J. Amer. Chem. Soc.*, 1951, **73**, 3518; Haszeldine, *J.*, 1952, 3423; 1954, 1273.
[20] McBee and Rapkin, *J. Amer. Chem. Soc.*, 1951, **73**, 1366.
[21] Burdon and Tatlow, *J. Appl. Chem.*, 1958, **8**, 293.
[22] Fales, *J. Amer. Chem. Soc.*, 1955, **77**, 5118.

2 : 4-dinitrophenylhydrazone but rather poor elemental analyses were obtained for the free aldehyde. The aldehyde bisulphite compound was converted in poor yield into 2 : 3 : 4 : 5 : 6-pentafluoromandelonitrile by sodium cyanide in water.

Experimental

Preparation of Pentafluorobenzene.—In a typical experiment, the 1*H* : 4*H*/2*H* : 5*H*-octafluoro*cyclo*hexane (58·0 g.; b. p. 118°) was dehydrofluorinated with potassium hydroxide (116 g.) and water (116 c.c.) as described before.[13] The mixture of four products was separated by gas chromatography to give pentafluorobenzene (24·0 g.), b. p. 85°. It had infrared absorptions associated with the benzene ring at 1535 and 1512 cm.$^{-1}$. The three other octafluoro*cyclo*hexanes,[13] b. p. 125°, 133°, and 136°, also gave pentafluorobenzene on dehydrofluorination.

1 : 2 : 3 : 4 : 5 : 6-*Hexachloro*-1 : 2 : 3 : 4 : 5-*pentafluoro*cyclo*hexane.*—Pentafluorobenzene (2·2 g.) and liquid chlorine (3·5 g.) were shaken together in a sealed tube which was irradiated with ultraviolet light at room temperature for 46 hr. The tube was then cooled in liquid oxygen and opened. Chlorine was allowed to evaporate and the residue was washed with sodium metabisulphite solution, to leave a viscous oil (4·3 g.), distillation of which *in vacuo* gave 1 : 2 : 3 : 4 : 5 : 6-*hexachloro*-1 : 2 : 3 : 4 : 5-*pentafluoro*cyclo*hexane*, b. p. 92°/0·5 mm. (Found: C, 19·0; H, 0·2; F, 25·2. $C_6HCl_6F_5$ requires C, 18·9; H, 0·3; F, 24·9%). An infrared absorption peak at *ca.* 2950 cm.$^{-1}$ was characteristic of a C–H bond. There were no C=C bands.

Pentafluorobenzenesulphonic Acid.—A mixture of pentafluorobenzene (6·8 g.) and fuming sulphuric acid (168 g.; 20% of sulphur trioxide) was kept at 15° for 48 hr., then poured on crushed ice, and the aqueous solution was extracted continuously with ether for 24 hr. The extract was dried ($MgSO_4$), filtered, and evaporated to leave a dark brown oil which was dissolved in a small volume of water and neutralised with barium carbonate. The hot solution was filtered and cooled, to give crystalline barium pentafluorobenzenesulphonate (11·2 g.). Small portions of the crude acid were converted into the S-*benzylthiuronium salt*, m. p. 176—178° (from water) (Found: C, 40·3; H, 2·5. $C_{14}H_{11}O_3N_2S_2F_5$ requires C, 40·6; H, 2·7%), and the *anilinium salt*, m. p. 298—300° (decomp.) (from acetone–chloroform) (Found: C, 42·3; H, 2·5. $C_{12}H_8O_2NSF_5$ requires C, 42·2; H, 2·4%). The free acid was prepared by precipitation of the barium as the sulphate with an equivalent amount of dilute sulphuric acid and evaporation of the aqueous solution. It formed low-melting (*ca.* 30°), extremely hygroscopic crystals which appeared to decompose at room temperature during a week. Evaporation of the aqueous solution of the sodium salt was rendered difficult by production of a foam; this, however, quickly collapsed.

Bromopentafluorobenzene.—Pentafluorobenzene (11·2 g.) was added to a stirred mixture of bromine (6·8 c.c.), 20% oleum (30 c.c.), and anhydrous aluminium tribromide (0·6 g.) at room temperature. The mixture was stirred and heated at 60—65° for 4 hr., then poured on ice (*ca.* 200 g.), and the lower layer was separated, washed with aqueous sodium carbonate, sodium metabisulphite, and water. Distillation from phosphoric oxide gave bromopentafluorobenzene (13·3 g.), b. p. 134—135°, n_D^{19} 1·4505 (Found: C, 29·2; F, 38·9. Calc. for C_6BrF_5: C, 29·2; F, 38·5%), $\lambda_{max.}$ 2430 Å (ε 887; concn. 0·1022 g./l. in ethanol).

Pentafluoroiodobenzene.—Pentafluorobenzene (11·2 g.) was iodinated, by the procedure described above, with iodine (24 g.) and 20% oleum (40 c.c.), to give *pentafluoroiodobenzene* (13·9 g.), b. p. 161—163°, n_D^{19} 1·4970 (Found: C, 24·6; F, 32·1. C_6F_5I requires C, 24·5; F, 32·3%), $\lambda_{max.}$ 2600 Å (ε 1081; concn. 0·1044 g./l. in ethanol).

Decafluorodiphenyl.—Bromopentafluorobenzene (2·00 g.) and activated copper bronze (2·00 g.) were heated together in a sealed tube at 200° for 42 hr. The product was extracted with ether, and the extracts were evaporated, to leave a white solid which, recrystallised from benzene, gave *decafluorodiphenyl* (1·15 g.), m. p. 68—69° (Found: C, 42·8; F, 56·9. $C_{12}F_{10}$ requires C, 43·1; F, 56·9%), $\lambda_{max.}$ 2690 Å (ε 2446; concn. 0·086 g./l. in ethanol).

This fluorocarbon was mentioned [23] in a patent, but no properties or constants were given.

Pentafluorophenylmagnesium Bromide.—Bromopentafluorobenzene (2·47 g.) was added to magnesium turnings (0·30 g.) in dry ether (5 c.c.) and a small crystal of iodine added. The reaction started on slight warming and was completed by 2 hours' refluxing. Water (5 c.c.) was then added to the dark solution, followed by dilute sulphuric acid (5 c.c.). The ether layer was

[23] McBee, Lindgren, and Ligett, U.S.P. 2,488,216; *Chem. Abs.*, 1950, **44**, 1628.

separated, dried ($MgSO_4$), and shown to contain pentafluorobenzene by analytical gas chromatography. Most of the ether was removed by distillation through a 6″ vacuum-jacketed fractionating column packed with Dixon gauze spirals (1/16″ × 1/16″), and the residue was separated by preparative-scale gas chromatography (column A;[13] temp. 108°; N_2 flow-rate 9·4—9·6 l./hr.), to give pentafluorobenzene (0·9 g.), n_D^{18} 1·3931. This had an infrared absorption spectrum identical over the range 3000—700 cm.$^{-1}$ with that of an authentic specimen. *Deuteropentafluorobenzene* (0·75 g.), n_D^{20} 1·3906, was prepared also by this method, from bromopentafluorobenzene (2·50 g.) and magnesium (0·30 g.) in ether, followed by the addition of deuterium oxide (2·0 g.). This compound displayed an infrared C–D stretching frequency of 2315 cm.$^{-1}$, and a purity of *ca.* 98% was indicated by the strength of the pentafluorobenzene peak at 837 cm.$^{-1}$.

Pentafluorobenzoic Acid from the Grignard Reagent.—Pentafluoroiodobenzene (2·9 g.) was added to a suspension of magnesium turnings (0·24 g.) in dry ether (20 c.c.), followed by a crystal of iodine. The Grignard appeared to be slowly formed and reaction was completed by 5 hours' refluxing. Dry carbon dioxide was bubbled through the Grignard solution for 8 hr. To the mixture was added 50% v/v sulphuric acid (50 c.c.), and the whole was extracted continuously with ether for several days. The ether extract was then dried ($MgSO_4$), filtered, and evaporated to give pentafluorobenzoic acid (0·046 g.), m. p. 102° alone and mixed with a specimen prepared by the oxidation of pentafluorophenylethylene.

1-(*Pentafluorophenyl*)*ethanol.*—Bromopentafluorobenzene (7·5 g.) was added to magnesium turnings (0·9 g.) in dry ether (100 c.c.). The Grignard reaction was started by addition of a crystal of iodine and gentle heat; it was completed by 1—2 hours' refluxing. Dry acetaldehyde (3·0 c.c.) in dry ether (30 c.c.) was added to the Grignard solution at 0°. The mixture was stirred for 16 hr. at 15°, then decomposed with dilute hydrochloric acid (50 c.c.). The aqueous layer was extracted several times with ether. The combined ethereal extracts were dried ($MgSO_4$) and distilled through a vacuum-jacketed column (6″ × ½″) packed with Dixon spirals, and the residue distilled under slightly reduced pressure. Redistillation of the product gave 1-(*pentafluorophenyl*)*ethanol* (4·4 g.), b. p. 68—70°/30 mm., n_D^{18} 1·4402 (Found: C, 45·6; H, 2·6. $C_8H_5OF_5$ requires C, 45·3; H, 2·4%). The alcohol (0·2 g.) and 3 : 5-dinitrobenzoyl chloride (0·5 g.) were kept at 100° for 1 hr. in pyridine (2 c.c.). Water (5 c.c.) was added and the mixture poured into sodium hydrogen carbonate solution and extracted with ether. The ethereal extract was washed with dilute hydrochloric acid, dried ($MgSO_4$), filtered, and evaporated and the residue recrystallised from ethanol, to give 1-(*pentafluorophenyl*)*ethyl* 3 : 5-*dinitrobenzoate* (0·16 g.), m. p. 83° (Found: C, 44·0; H, 1·9. $C_{15}H_7O_6N_2F_5$ requires C, 44·3; H, 1·7%).

Pentafluorophenylethylene.—1-(Pentafluorophenyl)ethanol (3·5 g.), phosphoric oxide (1·5 g.) and quinol (0·1 g.) were heated together at 160° for 1 hr. The product was distilled out under slightly reduced pressure and redistilled, to give *pentafluorophenylethylene* (2·0 g.), b. p. 139—140°, n_D^{22} 1·4444 (Found: C, 49·4; H, 1·6. $C_8H_3F_5$ requires C, 49·5; H, 1·6%), $\lambda_{max.}$ 2340 and 2410 Å (ε 8364 and 9105, respectively; concn. 0·0078 g./l. in ethanol).

1 : 2-*Dibromo*-1-*pentafluorophenylethane.*—Bromine (0·4 c.c.) in dry ether (25 c.c.) was added to a solution of pentafluorophenylethylene (1·4 g.) in dry ether (25 c.c.) at 0°. The mixture was kept at 15° for 15 hr. and the excess of bromine then destroyed by sodium metabisulphite solution. The ether layer was separated, dried ($MgSO_4$), filtered, and evaporated to leave a liquid product which was distilled twice from phosphoric oxide to give 1 : 2-*dibromo*-1-*pentafluorophenylethane* (1·52 g.), b. p. 75—80°/0·5 mm. (Found: C, 27·2; H, 0·8. $C_8H_3Br_2F_5$ requires C, 27·1; H, 0·9%).

Attempted Addition of Water to Pentafluorophenylethylene.—No reaction was observed between pentafluorophenylethylene (0·9 g.) and 50% v/v sulphuric acid (18 c.c.) after 10 hours' refluxing. When shaken at 100° for 24 hr. in a sealed tube these reactants gave a polymeric material (0·4 g.). The aqueous phase was extracted continuously with ether but the extract left no residue on evaporation.

Pentafluorobenzoic Acid from Pentafluorophenylethylene.—Pentafluorophenylethylene (1·2 g.), potassium permanganate (3·0 g.), and dry acetone (50 c.c.) were shaken together at 15° for several hr. and then kept at 15° for 15 hr. Water was added and the acetone removed at reduced pressure. Unchanged permanganate and manganese dioxide were destroyed with sulphur dioxide, concentrated sulphuric acid (15 c.c.) was added, and the solution was extracted continuously with ether for 15 hr. The extract was dried ($MgSO_4$), filtered, and evaporated to leave a solid which recrystallised from toluene–light petroleum (b. p. 100—120°) as square

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plates of pentafluorobenzoic acid (0·52 g.), m. p. 103—104°, $\lambda_{max.}$ 2650 Å (ε 761; concn. 0·011 g./l. in water) (Found: C, 39·9; H, 0·5. Calc. for $C_7HO_2F_5$: C, 39·6; H, 0·5%).

The acid (0·09 g.) was dissolved in water and neutralised with sodium hydroxide, and the pH adjusted to 4 with hydrochloric acid. An aqueous solution of *S*-benzylthiuronium chloride was added, and the precipitate recrystallised from water, to give S-*benzylthiuronium pentafluorobenzoate* (0·13 g.), m. p. 178° (Found: C, 47·8; H, 3·2. $C_{15}H_{11}O_2N_2SF_5$ requires C, 47·6; H, 2·9%). An m. p. of 106—107° has been given [20] for the acid.

Pentafluorobenzaldehyde.—(*a*) Bromopentafluorobenzene (5·0 g.) was added to magnesium turnings (0·8 g.) in dry ether (100 c.c.), the reaction being initiated by iodine and completed by 2 hours' refluxing. Ethyl orthoformate (3·5 g.) was then added and the mixture heated under reflux with stirring for 10 hr. The ether was removed and dilute sulphuric acid (30 c.c.) was added with stirring, followed by concentrated sulphuric acid (25 c.c.). After being heated under reflux for 3 hr. the mixture was distilled in steam, and a saturated aqueous solution of sodium metabisulphite added to the organic layer of the distillate to give crystalline pentafluorobenzaldehyde sodium bisulphite compound (1·9 g.).

(*b*) Bromopentafluorobenzene (4·5 g.) was added to magnesium turnings (0·7 g.) in dry, peroxide-free tetrahydrofuran (30 c.c.). The reaction was started by iodine and completed by 1 hour's refluxing. 3 : 4-Dihydro-6-methyl-3-*p*-tolylquinazoline methiodide (7 g.) was then added and the suspension refluxed with stirring for 9 hr. Dilute hydrochloric acid (50 c.c.) was added and the mixture was steam-distilled. The aqueous phase remaining was extracted continuously with ether for 24 hr., the extracts were dried ($MgSO_4$), filtered, and evaporated, and the residue was combined with the steam-distillate. Saturated aqueous sodium metabisulphite was added, to give a precipitate of pentafluorobenzaldehyde sodium bisulphite compound (1·8 g.).

The above yields of bisulphite compound could not be improved by changes in reaction time, temperature, or solvent.

(*c*) The bisulphite compound (3·8 g.) was heated under reflux for 1 hr. with 10% v/v sulphuric acid (30 c.c.). The solution was steam-distilled and the distillate extracted several times with ether. The combined extracts were dried ($MgSO_4$), filtered, and evaporated and the residue was distilled, to give pentafluorobenzaldehyde (1·4 g.), b. p. 168—170°, n_D^{17} 1·4505, $\lambda_{max.}$ 2350, 2430 Å (ε 17,330, 14,780, respectively; concn. 0·0068 g./l. in *n*-hexane) (Found: C, 42·0; H, 0·7. Calc. for C_7HOF_5: C, 42·9; H, 0·5%).

The aldehyde was added to an alcoholic solution of 2 : 4-dinitrophenylhydrazine and after ½ hr. water was added. A yellow precipitate was obtained which was recrystallised from ethanol, to give *pentafluorobenzaldehyde* 2 : 4-*dinitrophenylhydrazone*, m. p. 229—230° (Found: C, 41·7; H, 1·6. $C_{13}H_5O_4N_4F_5$ requires C, 41·5; H, 1·3%).

2 : 3 : 4 : 5 : 6-*Pentafluoromandelonitrile.*—Sodium cyanide (2·0 g.) in water (5 c.c.) was added, dropwise, to a stirred suspension of pentafluorobenzaldehyde sodium bisulphite compound (3·2 g.) and sodium metabisulphite (0·9 g.) in water (20 c.c.) at 0°. The suspension was stirred for 8 hr. at 0°, then extracted continuously with ether for 48 hr. The ether extract was dried ($MgSO_4$), filtered, and evaporated, to leave a brown syrupy residue which crystallised from benzene–light petroleum (b. p. 60—80°) to give 2 : 3 : 4 : 5 : 6-*pentafluoromandelonitrile* (0·09 g.), m. p. 53—54° (Found: C, 42·9; H, 1·1. $C_8H_2ONF_5$ requires C, 43·1; H, 0·9%).

Infrared Spectra.—These have been deposited in the Documentation of Molecular Spectra issued by Butterworths.

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32. *Phenolic Alkaloids occurring in* Lycoris radiata.

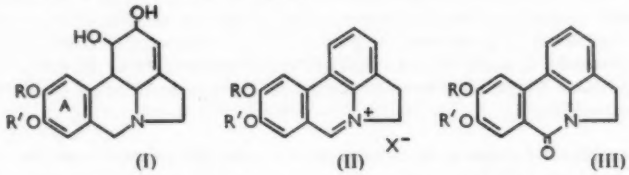
By Shojiro Uyeo and Noboru Yanaihara.

The position of the phenolic hydroxyl group in *pseudo*lycorine (I; R = H, R′ = Me) has been located by degradation of its ethyl ether, and by synthesis of the resulting phenanthridone (III; R = Et, R′ = Me).

Two new phenolic alkaloids, norpluviine and demethylhomolycorine have been isolated from *Lycoris radiata*, and shown to have structures (IV; R = Me, R′ = H) and (V; R = Me, R′ = H), respectively.

Kondo, Tomimura, and Ishiwata [1] reported in 1932 the isolation of a new phenolic base from the bulbs of *Lycoris radiata* and named it *pseudo*lycorine since they presumed that it possessed the same molecular formula as that of lycorine,[2] $C_{16}H_{17}O_4N$. For further characterisation they prepared derivatives such as the hydrochloride, methiodide, and acetate and showed also that the base contained one methoxyl and three hydroxyl groups, but no *N*-methyl group; however, no extensive degradations were undertaken. Nine years later, Professor Kondo generously provided one of us (S. U.) with the original material which made it possible for us to re-investigate this valuable alkaloid. We have found that analytical values of the base and its derivatives are in better agreement with the molecular formula $C_{16}H_{19}O_4N$ than with the previous one. Zinc dust distillation of the base yielded phenanthridine which suggested that the base might belong to the phenanthridine alkaloids, as does lycorine.[3] In order to elucidate the structure, however, it seemed desirable to secure additional quantities of the alkaloid, but no *pseudo*lycorine was ever obtained from extracts of the bulbs of *Lycoris radiata* procured in our vicinity and the problem remained dormant until 1956 when Fales, Giuffrida, and Wildman [4] demonstrated that the *O*-methyl derivative obtained by methylation of *pseudo*lycorine with diazomethane was identical with a new non-phenolic alkaloid occurring in the King Alfred daffodil. They named this new base methyl*pseudo*lycorin and assigned to it the structural formula (I; R = R′ = Me), so that *pseudo*lycorine must be represented by (I; R = H, R′ = Me or *vice versa*).

In order to locate the position of the hydroxyl group, *pseudo*lycorine was ethylated with diazoethane. The resulting *O*-ethyl derivative, when treated with phosphorus oxychloride, gave an anhydro-*O*-ethyl*pseudo*lycorinium salt [5] (II; R = Et; R′ = Me), the sparingly soluble iodide being most conveniently isolated. Oxidation of this salt with alkaline potassium ferricyanide afforded a lactam which was shown to be identical with the synthetic compound (III; R = Et, R′ = Me).



(I) (II) (III)

Both the lactam (III; R = Et, R′ = Me) and its isomer (III; R = Me, R′ = Et) were synthesised from the respective *N*-benzoyl dihydroindoles by the method previously used for preparation of the analogous 6 : 7-methylenedioxypyrrolinophenanthridone.[6]

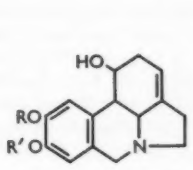
As well as *pseudo*lycorine, two more phenolic alkaloids have recently been isolated from

[1] Kondo, Tomimura, and Ishiwata, *J. Pharm. Soc. Japan*, 1932, **52**, 433.
[2] Kondo and Tomimura, *ibid.*, 1928, **48**, 223.
[3] Kondo and Uyeo, *Ber.*, 1935, **68**, 1756.
[4] Fales, Giuffrida, and Wildman, *J. Amer. Chem. Soc.*, 1956, **78**, 4145.
[5] Cf. Kondo, Takeda, and Kotera, *Ann. Report, Itsuu Lab.*, 1954, **5**, 66.
[6] Humber, Kondo, Kotera, Takagi, Takeda, Taylor, Thomas, Tsuda, Tsukamoto, Uyeo, Yajima, and Yanaihara, *J.*, 1954, 4622.

the same plant, namely norpluviine [7] and demethylhomolycorine. A concentrated methanolic solution of the phenolic fraction deposited crystals of norpluviine on storage for a long time, and the ethyl acetate-soluble fraction of the mother-liquor of norpluviine afforded demethylhomolycorine after chromatography over alumina.

Norpluviine has the formula $C_{15}H_{16}O_2N{\cdot}OMe$. It is soluble in aqueous sodium hydroxide and gives a violet ferric chloride test, indicating its phenolic character. With diazomethane it afforded the non-phenolic pluviine [7] (IV; R = R′ = Me). Norpluviine therefore has structure (IV; R = Me, R′ = H or *vice versa*). The correctness of the first possibility was established by degradation of *O*-ethylnorpluviine to the phenanthridone (III; R = Me, R′ = Et) as follows. *O*-Ethylnorpluviine, heated with acetic anhydride, gave, together with *O*-acetyl-*O*-ethylnorpluviine, an anhydrodehydro-*O*-ethylnorpluviinium salt (II; R = Me, R′ = Et) (pluviine behaved in the same way [7]). This was immediately converted by ferricyanide into the more conveniently identifiable lactam, m. p. 226—228°, identical with the synthetic phenanthridone (III; R = Me, R′ = Et) described above.

The further phenolic alkaloid, demethylhomolycorine, $C_{17}H_{19}O_4N$, was readily soluble in cold aqueous sodium hydroxide and gave a violet colour with ferric chloride. The ultraviolet absorption spectrum exhibited bands which were very similar to those of homolycorine and the infrared spectrum showed absorptions at 3·05 (OH), 5·89 (C=O), and 6·18 μ (aromatic ring) in agreement with expectation. Methylation with diazomethane converted this alkaloid into homolycorine, as shown by a mixed melting point and infrared spectra. While homolycorine contained two methoxyl groups, demethylhomolycorine was shown by analysis to have one, which lead us to propose formula (V; R = Me, R′ = H or *vice versa*) for the latter. A decision in favour of (V; R = Me, R′ = H) was made by the following degradation. Demethylhomolycorine was ethylated, then reduced with lithium aluminium hydride to the diol (VI; R = Me, R′ = Et). This was treated with



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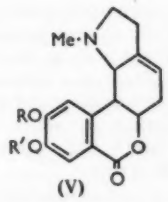

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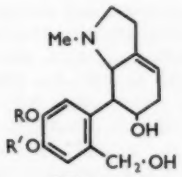

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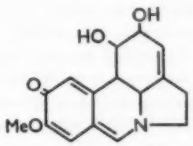

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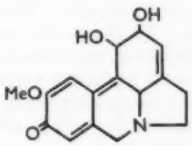

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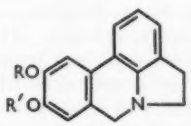

(IX)

toluene-*p*-sulphonyl chloride in pyridine and the product was processed in the manner used for conversion of tetrahydrohomolycorine into pluviine (forthcoming paper). Distillation *in vacuo* of the crude methochloride and purification of the distillate did not lead as expected to ethylnorpluviine, the only isolable product being the phenanthridone (III; R = Me, R′ = Et) formed apparently as a result of aerial oxidation of the intermediate, anhydrodehydro-*O*-ethylnorpluviine (IX; R = Me, R′ = Et). The amount of demethylethylhomolycorine at our disposal precluded a repetition of this experiment, but the isolation of the phenanthridone was sufficient to prove that demethylethylhomolycorine and demethylhomolycorine must be represented by the formulæ (V; R = Me, R′ = Et) and (V; R = Me, R = H), respectively.

[7] Boit, Ehmke, Uyeo, and Yajima, *Chem. Ber.*, 1957, **90**, 363.

It is interesting that *pseudo*lycorine, even in a glass tube, undergoes a colour change first to yellow and finally brown to black. We consider that this may be due to aerial oxidation to a compound having a quinonoid structure (VII) which then undergoes further changes. Since there appears to be no driving force for the formation of a quinone such as (VIII), this ready discoloration of *pseudo*lycorine is in accord with the position assigned to the free hydroxyl group in ring A of the base.

In contrast to *pseudo*lycorine, norpluviine and demethylhomolycorine are stable and do not colour appreciably on long storage.

Experimental

Ultraviolet absorption spectra were determined for 95% ethanol solutions on a Beckman DU spectrometer. Infrared spectra were taken on the Perkin-Elmer Model 21 in Nujol.

pseudo*Lycorine*.—*pseudo*Lycorine crystallised from water as needles, m. p. 247—248° (decomp.), $[\alpha]_D$ −62° (*c* 1·2 in EtOH) (lit.,[1] m. p. 245°) (Found: C, 53·1; H, 7·9; OMe, 8·8. $C_{16}H_{19}O_4N,4H_2O$ requires C, 53·2; H, 7·5; OMe, 8·6%), soluble in hot water, slightly soluble in acetone, chloroform, or methanol and very slightly soluble in ether. A solution of the base in cold aqueous sodium hydroxide deposited the base on addition of ammonium chloride. The alkaloid contains neither a *N*-methyl (Herzig–Meyer) nor a *C*-methyl (Kuhn–Roth) group. For analysis the hydrate was dried *in vacuo* over phosphoric oxide at 100° for 6 hr., after which the anhydrous *form* melted at 240—242° (Found: C, 66·4; H, 6·4; N, 5·1; OMe, 11·2. $C_{16}H_{19}O_4N$ requires C, 66·4; H, 6·6; N, 4·8; OMe, 10·7%). The *hydrochloride* crystallised from methanol as needles, m. p. 266° (decomp.) (lit.,[1] m. p. 261°) (Found: C, 59·0; H, 6·4; N, 4·6. $C_{16}H_{19}O_4N,HCl$ requires C, 59·0; H, 6·1; N, 4·3%). The *methiodide* crystallised from methanol–acetone as prisms, m. p. 250—252° (decomp.) (lit.,[1] 150°) (Found: C, 47·4; H, 5·3; I, 29·4. $C_{16}H_{19}O_4N,CH_3I$ requires C, 47·3; H, 5·1; I, 29·4%).

O-*Acetyl*pseudo*lycorine*.—*pseudo*Lycorine (0·1 g.) and anhydrous sodium acetate (0·1 g.) in acetic anhydride (3 ml.) were heated on a water-bath for 1·5 hr. The mixture was concentrated under reduced pressure, and the residue taken up in water, basified with aqueous ammonia, and extracted with chloroform. The chloroform extract gave on evaporation the *acetate* (70 mg.), plates (from methanol), m. p. 204—205° (lit.,[1] m. p. 98—101°), $[\alpha]_D$ +34·6° (*c* 0·5 in EtOH) (Found: C, 63·9; H, 6·0; Ac, 29·4. $C_{22}H_{25}O_7N$ requires C, 63·6; H, 6·1; Ac, 30·2%), $\lambda_{max.}$ 5·73 and 5·76 μ. The *acetate hydrochloride* was prepared by adding an ethereal solution of dry hydrogen chloride to acetyl*pseudo*lycorine in ether. Recrystallisation from methanol gave needles, m. p. 251° (decomp.) [lit.,[1] 272° (decomp.)] (Found: C, 52·3; H, 6·5. $C_{22}H_{25}O_7N,HCl,3H_2O$ requires C, 52·2; H, 6·4%).

Zinc Dust Distillation of pseudo*lycorine*.—A mixture of *pseudo*lycorine (0·4 g.) and zinc dust (10 g.) was distilled in an atmosphere of hydrogen. The distillate was taken up in ether and extracted with 5% hydrochloric acid. To the acidic aqueous layer was added a saturated solution of mercuric chloride. The resulting precipitate was dissolved in hot water, filtered from insoluble material, and treated with hydrogen sulphide to remove mercury. The clear filtrate was basified, and extracted with ether, which was then evaporated to dryness, and the residue was distilled in a vacuum. The distillate, b. p. 100—115° (bath-temperature)/0·1 mm., which solidified immediately, was converted into its picrate, m. p. 235°, undepressed on admixture with phenanthridine picrate, m. p. 245° (Found: C, 56·1; H, 3·1. Calc. for $C_{13}H_9N,C_6H_3O_7N_3$: C, 55·9; H, 3·0%).

O-*Methyl*pseudo*lycorine*.—To a solution of *pseudo*lycorine (0·1 g.) in ethanol (25 ml.) was added excess of ethereal diazomethane, and the mixture was set aside at room temperature for 10 days. After evaporation, the *ether* (62 mg.) which was insoluble in hot water was crystallised from methanol, to give prisms, m. p. 241° (decomp.), $[\alpha]_D$ −72·5° (*c* 0·4 in MeOH) (lit.,[4] m. p. 234—242°) (Found: C, 67·5; H, 7·1; OMe, 20·3. $C_{17}H_{21}O_4N$ requires C, 67·3; H, 7·0; OMe, 20·5%).

O-*Ethyl*pseudo*lycorine*.—*pseudo*Lycorine (70 mg.) in methanol (15 ml.) was treated with excess of ethereal diazoethane and after 2 days the mixture was concentrated and treated again with additional solution of diazoethane for a further day. After being washed with aqueous sodium hydroxide, the mixture was concentrated to give a residue (45 mg.) which was purified by chromatography in chloroform–ethanol (10 : 1) on alumina. Crystallisation of the eluted material (30 mg.) from methanol gave colourless prisms of the *ether*, m. p. 242° (decomp.), $[\alpha]_D$ −68·6° (*c* 0·35 in EtOH) (Found: C, 68·6; H, 7·2. $C_{18}H_{23}O_4N$ requires C, 68·1; H, 7·3%).

XUM

Formation of the Phenanthridone (III; R = Et, R′ = Me).—*O*-Ethyl*pseudo*lycorine (20 mg.) and phosphorus oxychloride (0·5 ml.) were heated on a water-bath for 1 hr. Ice-water (2 ml.) was added to the mixture and the solution saturated with potassium iodide to precipitate anhydro-*O*-ethyl*pseudo*lycorinium iodide. This salt (16 mg.), potassium ferricyanide (25 mg.), and potassium hydroxide (25 mg.) in 50% ethanol (2 ml.) were heated on a water-bath. Crystals began to separate in 10 min. and the reaction was complete in 1 hr. The precipitate was extracted with chloroform, and the chloroform extract washed with dilute hydrochloric acid and water, dried, and evaporated to give a residue (3 mg.) which was purified by sublimation at 160—190° (bath-temperature)/0·1 mm., followed by crystallisation from methanol; it then had m. p. 175—177°, undepressed upon admixture with synthetic 6-ethoxy-7-methoxypyrrolino-(3′ : 2′ : 1′-1 : 10a : 10)phenanthridone (III; R = Et, R′ = Me) as described below. The ultraviolet and infrared spectra of both the natural and the synthetic product were identical.

4-Ethoxy-5-methoxy-2-nitrobenzoic Acid.—*O*-Ethylvanillic acid (7·5 g.) was nitrated with nitric acid (32 ml.; *d* 1·52) with stirring for 1 hr. at 20—30°. The mixture was poured into ice-water, and the yellow precipitate collected and extracted with saturated sodium hydrogen carbonate solution. The insoluble material (2 g.) was filtered off and the clear solution when acidified with hydrochloric acid gave crude *4-ethoxy-5-methoxy-2-nitrobenzoic acid* (5·2 g.) which crystallised from methanol as pale yellow needles, m. p. 172—174° (Found: C, 50·0; H, 4·6; N, 5·6. $C_{10}H_{11}O_6N$ requires C, 49·8; H, 4·6; N, 5·8%). The insoluble material mentioned above, *1-ethoxy-2-methoxy-3 : 5-dinitrobenzene*, crystallised from ethanol in yellow leaflets, m. p. 143—145° (Found: C, 45·0; H, 4·1; N, 11·2. $C_9H_{10}O_6N_2$ requires C, 44·6; H, 4·2; N, 11·6%).

1-(4-Ethoxy-5-methoxy-2-nitrobenzoyl)-2 : 3-dihydroindole.—To a stirred solution of 2 : 3-dihydroindole (0·75 g.) and pyridine (5 ml.) in chloroform (15 ml.) was added dropwise a solution of 4-ethoxy-5-methoxy-2-nitrobenzoyl chloride (from 1·7 g. of acid and excess of thionyl chloride) in chloroform (10 ml.) during 30 min. and the mixture refluxed on a water-bath for 2 hr. Next morning the chloroform solution was washed successively with 5% hydrochloric acid, 5% sodium hydroxide solution, and water, dried, and evaporated to a solid (1·7 g.) which on crystallisation from methanol gave the pure *nitro-amide* as pale yellow needles, m. p. 167—168° (Found: C, 63·4; H, 5·6; N, 8·1. $C_{18}H_{18}O_5N_2$ requires C, 63·2; H, 5·3; N, 8·2%).

1-(2-Amino-4-ethoxy-5-methoxybenzoyl)-2 : 3-dihydroindole.—The nitro-amide (1·65 g.) obtained as above was reduced catalytically in ethyl acetate (30 ml.) in the presence of palladium–carbon (0·6 g.; 1 : 5). The mixture was filtered and evaporated to dryness and the residue dissolved in 5% hydrochloric acid, washed with ether, basified with sodium carbonate solution, and extracted with chloroform. Removal of the chloroform gave a solid (1·3 g.) which crystallised from ethanol to give the *amino-amide* as prisms, m. p. 137—138° (Found: C, 69·1; H, 6·3; N, 9·1. $C_{18}H_{20}O_3N_2$ requires C, 69·2; H, 6·5; N, 9·0%).

Pschorr Cyclisation of the Amino-amide.—The amino-amide (0·5 g.) was diazotised in 5% sulphuric acid (35 ml.) and methanol (10 ml.) with 5% sodium nitrite solution (10 ml.) at 0—5° and the whole kept for 1 hr. at room temperature. The temperature was then raised to 75—80° for 2 hr., and finally to 100° for 1 hr., an oil separating which was extracted with chloroform after cooling. The chloroform extract was washed with 5% sodium hydroxide solution, then with water, dried, and evaporated to an oil (0·42 g.) which was chromatographed over alumina. Elution with chloroform gave *1-(4-ethoxy-3-methoxybenzoyl)indole* which on crystallisation from ethanol formed prisms, m. p. 113—114°, $\lambda_{max.}$ 250 and 305 mμ (log ε 4·31 and 4·13) (Found: C, 73·2; H, 5·8; N, 4·7. $C_{18}H_{17}O_3N$ requires C, 73·2; H, 5·8; N, 4·7%). Hydrolysis of this product in 5% sodium hydroxide solution afforded indole (identified as its picrate, m. p. and mixed m. p. 159—160°) and *O*-ethylvanillic acid, m. p. and mixed m. p. 193—194°. Further elution with the same solvent gave *6-ethoxy-7-methoxypyrrolino*(3′ : 2′ : 1′-1 : 10*a* : 10)*phenanthridone* (40 mg.). After crystallisation from methanol, followed by sublimation in a vacuum and recrystallisation from methanol, it formed needles and had m. p. 176—177°, $\lambda_{max.}$ 250, 271, 325, and 340 mμ (log ε 4·58, 4·35, 3·81, and 3·88) (Found: C, 72·9; H, 5·9; N, 4·9. $C_{18}H_{17}O_3N$ requires C, 73·2; H, 5·8; N, 4·7%).

5-Ethoxy-4-methoxy-2-nitrobenzaldehyde.—6-Nitro*iso*vanillin (5 g.) in 10% sodium hydroxide solution (25 ml.) was ethylated with diethyl sulphate (6 g.) with stirring on a water-bath for 3 hr. After cooling, the precipitate (5·6 g.) was collected and crystallised from ethanol; the *aldehyde* had m. p. 160—161° (Found: C, 53·2; H, 4·8. $C_{10}H_{11}O_5N$ requires C, 53·3; H, 4·9%).

5-Ethoxy-4-methoxy-2-nitrobenzoic Acid.—To a stirred mixture of the above nitro-aldehyde (5·2 g.) in benzene (70 ml.) with sodium hydroxide (4 g.) in water (60 ml.) was added dropwise

an aqueous solution (200 ml.) of potassium permanganate (3 g.) at 70—80°. After the oxidising agent had been consumed, the mixture was filtered hot. The aqueous layer was acidified with hydrochloric acid, and the pale yellow *acid* (4·3 g.) which separated collected and crystallised from ethanol as yellow prisms, m. p. 215—216° (Found: C, 49·5; H, 4·4; N, 5·6. $C_{10}H_{11}O_6N$ requires C, 49·8; H, 4·6; N, 5·8%).

1-(*5-Ethoxy-4-methoxy-2-nitrobenzoyl*)-2 : 3-*dihydroindole*.—To a stirred solution of dihydroindole (1·1 g.) in pyridine (6 ml.) and chloroform (50 ml.) was added dropwise (30 min.) a solution of 5-ethoxy-4-methoxy-2-nitrobenzoyl chloride (from 2·6 g. of acid and excess of thionyl chloride) in chloroform (15 ml.). After a further 2 hours' refluxing and cooling, the chloroform solution was washed with 5% hydrochloric acid, then with 5% aqueous sodium hydroxide and water, and dried. Evaporation of the chloroform gave a solid *derivative* (2·95 g.) which crystallised from methanol as pale yellow needles, m. p. 176—177° (Found: C, 63·4; H, 5·5; N, 8·2. $C_{18}H_{18}O_5N_2$ requires C, 63·2; H, 5·3; N, 8·2%).

1-(*2-Amino-5-ethoxy-4-methoxybenzoyl*)-2 : 3-*dihydroindole*.—The preceding nitro-amide (1·3 g.) was reduced in chloroform with hydrogen in the presence of palladium–carbon and, after working up, 1-(*2-amino-5-ethoxy-4-methoxybenzoyl*)-2 : 3-*dihydroindole* (1·15 g.) was obtained. Crystallisation from light petroleum (b. p. 40—60°) gave prisms, m. p. 100—101° (Found: C, 68·9; H, 6·5; N, 9·1. $C_{18}H_{20}O_3N_2$ requires C, 69·2; H, 6·5; N, 9·0%).

Pschorr Cyclisation of the Preceding Amino-amide.—The amino-amide (0·5 g.) obtained above was diazotised in 5% sulphuric acid (30 ml.). On working up as described above, two products were isolated after chromatography over alumina. The first eluate (190 mg.) gave 1-(*3-ethoxy-4-methoxybenzoyl*)*indole*, needles, m. p. 122—123° (from ethanol), $\lambda_{max.}$ 250 and 305 mμ (log ε 4·37 and 4·15) (Found: C, 72·9; H, 5·9; N, 4·8. $C_{18}H_{17}O_3N$ requires C, 73·2; H, 5·8; N, 4·7%); the second (40 mg.) afforded 7-*ethoxy*-6-*methoxypyrrolino*(3′ : 2′ : 1′-1 : 10*a* : 10)-*phenanthridone* which on sublimation at 180—210° (bath-temperature)/0·1 mm. and crystallisation from methanol formed needles, m. p. 229—230°, $\lambda_{max.}$ 250, 271, 325, and 340 mμ (log ε 4·63, 4·48, 3·91, and 3·98) (Found: C, 73·0; H, 5·9; N, 4·6. $C_{18}H_{17}O_3N$ requires C, 73·2; H, 5·8; N, 4·7%).

Norpluviine.—The crude alkaloids extracted from the bulbs of *Lycoris radiata* were dissolved in chloroform and extracted with 2% aqueous sodium hydroxide. The aqueous layer was made ammoniacal by the addition of ammonium carbonate and extracted with chloroform. After evaporation of the chloroform, the residue was triturated with a little methanol and kept at room temperature for a week or longer, a solid *alkaloid* being precipitated which was collected and crystallised from water or ethanol to give needles or prisms, m. p. 274—275° (decomp.), $[\alpha]_D$ −160° (*c* 0·15 in MeOH) (Found: C, 70·2; H, 6·8; N, 5·4; OMe, 11·7. $C_{16}H_{19}O_3N$ requires C, 70·3; H, 7·0; N, 5·1; OMe, 11·4%).

O-*Methylnorpluviine*.—Norpluviine (60 mg.) in methanol (25 ml.) was treated with excess of an ethereal solution of diazomethane for 2 days. The mixture was then concentrated and an additional fresh diazomethane solution was added. After 24 hr., the mixture was evaporated, and the residue redissolved in chloroform, washed with aqueous sodium hydroxide, dried, and filtered through alumina. The filtrate gave on evaporation a solid which when crystallised from ethanol formed prisms and had m. p. 225—226°, undepressed on admixture with pluviine, $[\alpha]_D$ −181° (*c* 0·3 in EtOH) (Found: C, 70·9; H, 7·3. Calc. for $C_{17}H_{21}O_3N$: C, 71·0; H, 7·4%). The infrared spectrum was identical with that of pluviine.

O-*Ethylnorpluviine*.—Norpluviine (100 mg.) in methanol (30 ml.) was ethylated with diazoethane in the usual way; the resulting O-*ethyl derivative* crystallised from acetone as prisms, m. p. 148—149°, $[\alpha]_D$ −186° (*c* 0·28 in EtOH) (Found: C, 71·5; H, 7·7; N, 4·7; OMe + OEt, 25·3. $C_{18}H_{23}O_3N$ requires C, 71·7; H, 7·7; N, 4·7; OMe + OEt, 25·2%).

O-*Acetyl*-O-*ethylnorpluviine*.—*O*-Ethylpluviine (50 mg.) in acetic anhydride (2 ml.) was heated on a water-bath for 3 hr. Excess of acetic anhydride was removed by distillation under reduced pressure and the residue dissolved in 5% hydrochloric acid. The solution was basified with aqueous ammonia and extracted with ether, a small amount of insoluble material (5 mg.) remaining. The ethereal extract afforded *O*-acetyl-*O*-ethylnorpluviine (40 mg.) which crystallised from ether as needles, m. p. 185—186°, $[\alpha]_D$ −133° (*c* 0·3 in EtOH) (Found: C, 69·6; H, 7·3; N, 4·3. $C_{20}H_{25}O_4N$ requires C, 70·0; H, 7·3; N, 4·1%).

Formation of an Anhydrodehydro-O-*ethylnorpluviinium Salt and its Oxidation*.—*O*-Acetyl-*O*-ethylnorpluviine (55 mg.) in acetic anhydride (2 ml.) was heated at 130—140° for 3 hr. After evaporation of the excess of acetic anhydride in a vacuum, water was added, the mixture

basified with aqueous ammonia, and the precipitate extracted with chloroform. The chloroform was evaporated to dryness and the residue extracted with ether to remove unchanged acetylethylnorpluviine (11 mg.). The insoluble material (15 mg.) which remained undissolved in ether was oxidised in aqueous ethanol (10 ml.) with potassium ferricyanide (50 mg.) at water-bath temperature for 3 hr. After cooling, the mixture was extracted with chloroform, and the chloroform extract dried and concentrated to an oil which was distilled at 180—220° (bath-temperature)/0·1 mm. The distillate was crystallised from ethanol to give needles, m. p. 226—228°, identical with 7-ethoxy-6-methoxypyrrolino(3′ : 2′ : 1′-1 : 10a : 10)phenanthridone as shown by its mixed m. p. and infrared spectrum.

Demethylhomolycorine.—The mother-liquor (30 g.) from *Lycoris radiata*, from which the norpluviine had been obtained above, was extracted with ethyl acetate (100 ml.) on a water-bath, and the extract after concentration to 50 ml. was chromatographed over alumina. The ethyl acetate eluate gave on concentration a residue (2·5 g.) which was triturated with ethyl acetate, yielding *demethylhomolycorine* as colourless needles (300 mg.). Further elution with acetone, chloroform, and ethanol gave no crystalline compound. Demethylhomolycorine crystallised from ethyl acetate or hot water as needles, m. p. 213—214°, $[\alpha]_D$ +96·4° (*c* 0·28 in $CHCl_3$), $\lambda_{max.}$ 229, 269, and 307 mμ (log ε 4·32, 3·88, and 3·73), 3·05 μ (OH), 5·88 μ (C=O) (Found: C, 67·8; H, 6·2; N, 4·6; OMe, 10·5. $C_{17}H_{19}O_4N$ requires C, 67·8; H, 6·4; N, 4·7; OMe, 10·3%).

Demethyl-O-methylhomolycorine.—Demethylhomolycorine (100 mg.) in methanol (15 ml.) was methylated with ethereal diazomethane, furnishing homolycorine (95 mg.), m. p. and mixed m. p. 174—175° (from methanol), $[\alpha]_D$ +94·1° (*c* 0·51 in chloroform), $\lambda_{max.}$ 225, 269, and 303 mμ (log ε 4·36, 3·97, and 3·79), 5·82 μ (C=O) (Found: C, 68·2; H, 6·6; N, 4·4. Calc. for $C_{18}H_{21}O_4N$: C, 68·6; H, 6·7; N, 4·4%).

Demethyl-O-ethylhomolycorine.—Demethylhomolycorine (0·2 g.) in methanol (10 ml.) with diazoethane afforded the *ethyl derivative* (0·17 g.) as needles (from ethyl acetate–ether), m. p. 203—204°, $[\alpha]_D$ +95·2° (*c* 0·2 in $CHCl_3$) (Found: C, 68·8; H, 6·9; N, 4·3. $C_{19}H_{23}O_4N$ requires C, 69·3; H, 7·0; N, 4·3%).

Demethyl-O-ethyltetrahydrohomolycorine.—Demethyl-*O*-ethylhomolycorine (0·3 g.) in tetrahydrofuran (8 ml.) was heated on a water-bath with lithium aluminium hydride (0·2 g.) for 4 hr. After cooling, excess of lithium aluminium hydride was destroyed by the addition of a few drops of water, and the precipitate was filtered off and washed with tetrahydrofuran. The filtrate and washings were combined and evaporated to dryness and the residual *diol* (0·28 g.) crystallised from acetone, to give colourless prisms, m. p. 195—196° (Found: C, 68·1; H, 7·9; N, 4·3. $C_{19}H_{27}O_4N$ requires C, 68·4; H, 8·2; N, 4·2%).

Conversion of Demethyl-O-ethyltetrahydrohomolycorine into 7-Ethoxy-6-methoxypyrrolino-(3′ : 2′ : 1′-1 : 10a : 10)phenanthridone.—The above product (0·2 g.) and toluene-*p*-sulphonyl chloride (0·18 g.) in pyridine (10 ml.) was set aside overnight at room temperature and then heated on a water-bath for 1 hr. Pyridine was removed in a vacuum, and the residue taken up in water (10 ml.) and washed with ether. The aqueous layer was filtered through Amberlite IRA-400 ion-exchange resin, and the filtrate evaporated to dryness, taken up again in water, neutralised with hydrochloric acid, evaporated to dryness, and distilled [180—240° (bath)/0·01 mm.]. The distillate (20 mg.) was chromatographed in chloroform over alumina, and the first eluate was redistilled to give a product which after crystallisation from ethanol melted at 94—96°, $\lambda_{max.}$ 273, and 344 mμ (log ε 4·56 and 4·07). Although the amount of the product was insufficient for analysis, it appeared to be anhydrodehydro-*O*-ethylnorpluviine (IX; R = Me, R′ = Et) on the ground that its spectrum was very similar to that of anhydrodehydropluviine (IX; R = R′ = Me). The second eluate afforded 7-ethoxy-6-methoxypyrrolino(3′ : 2′ : 1′-1 : 10a : 10)phenanthridone which had m. p. and mixed m. p. 226—228° after sublimation at 180—210° (bath)/0·01 mm. followed by crystallisation from methnol. The ultraviolet and infrared spectra were also identical with those of an authentic sample described above.

We are grateful to Professor H. Kondo for a generous supply of *pseudo*lycorine which made this work possible, Dr. W. I. Taylor for reading the manuscript, and Messrs. Ikemoto and Takagishi, who were students of this school, for technical assistance in synthesising the phenanthridones.

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XUM

33. *Physical Properties of Anthraquinone and its Derivatives. Part I. Infrared Spectra.*

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The infrared spectra between 2 and 15 μ of anthraquinone and fifty-nine derivatives of it are reported, and correlations to assist the identification of unlisted anthraquinones are discussed.

In a survey by Briggs *et al.*[1] of the colouring matters of the *Coprosma* genus, various new hydroxyanthraquinones were isolated. To aid the elucidation of their structure, an investigation of the physical properties of hydroxy- and other substituted anthraquinones is being made. In this paper the infrared absorption spectra of anthraquinone and fifty-nine of its derivatives are reported and, where possible, correlations are made between the structure and observed absorption pattern. It is hoped to submit later reports on ultraviolet absorption spectra, half-wave potentials, and chromatographic properties of this series.

Experimental.—The anthraquinones were mostly natural products but some were of commercial origin. Derivatives without hydroxyl groups were purified by crystallization, but hydroxyanthraquinones were also purified by previous chromatography on columns of magnesia or magnesium carbonate. The spectra were recorded between 2 and 15 μ on a Beckman IR-2 spectrophotometer with rock-salt monochromator, the samples being prepared as paraffin mulls because of the low solubility of hydroxyanthraquinones in any suitable solvent.

Results and Discussion.—The sixty anthraquinones with their observed absorption bands are listed in Table 1. Spectra of anthraquinone derivatives having the same substitution pattern were found to be similar, regardless of the substituents, provided these compounds contained no hydroxyl groups. Hence compounds without hydroxyl groups are arranged first in the Table. β-Hydroxy-derivatives which show, in addition, absorption in the O–H stretching region are listed next; α-hydroxy-derivatives, in which the substitution pattern of the spectra is strongly modified, are given last. Bands arising in the regions of the C–H stretching and bending vibrations at around 3000 cm.$^{-1}$ and between 1480 and 1360 cm.$^{-1}$ are omitted because of the difficulty of measuring these in the presence of the paraffin mulling agent.

The hydroxyl and carbonyl stretching regions of absorption have been most often investigated by other workers, and a correlation between spectra in these regions and constitution has enabled certain limited groupings of anthraquinones to be made, thus assisting in their identification. The results in Table 1 extend the value of their correlations considerably. In the hydroxyl region they show that anthraquinones with one hydroxyl group in the β-position on the nucleus, or attached to a substituent group, all have one hydroxyl stretching band. The appearance of more than one hydroxyl band between 3600 and 3150 cm.$^{-1}$ indicates more than one such hydroxyl group attached to the anthraquinone nucleus, although the reverse does not always hold. More than one hydroxyl band appears only when two β-hydroxyl groups are adjacent or when β-hydroxyl groups are in a different environment, one in the normal position on the anthraquinone ring, and the other attached through a side chain or adjacent to some other α- or β-hydroxyl group.

α-Hydroxyl groups attached to the nucleus apparently show no hydroxyl absorption in a spectrum of a mulled sample. This was noted first in the overtone region by Hilbert, Wulf, Hendricks, and Liddel [2] and later by Flett,[3] working with the rock-salt region. The same effect was found by Johnson, Quayle, Robinson, Sheppard, and Todd [4] for hydroxy-derivatives of the extended quinones, but their investigation of a few simple α-hydroxyanthraquinones revealed a weak, broad absorption band with its centre near 2700 cm.$^{-1}$ which they assigned to the O–H stretching vibration. Hadži and Sheppard,[5] working with perfluorokerosene mulls, assigned a broad strong peak at 2900 cm.$^{-1}$, usually hidden by the paraffin mulling agent,

[1] Briggs and his co-workers, "Chemistry of the *Coprosma* Genus," Parts I—X, Part X (*J.*, 1955, 3298 and earlier papers).
[2] Hilbert, Wulf, Hendricks, and Liddel, *J. Amer. Chem. Soc.*, 1936, **58**, 548.
[3] Flett, *J.*, 1948, 1441.
[4] Johnson, Quayle, Robinson, Sheppard, and Todd, *J.*, 1951, 2633.
[5] Hadži and Sheppard, *Trans. Faraday Soc.*, 1954, **50**, 911.

XUM

TABLE 1. *Spectra of paraffin mulls of anthraquinones.*

No.	Anthraquinone	Frequency of infrared bands																
1	Unsubst.							1675s		1572m			1333s	1305w	1284s		1209w	
	Monosubstituted anthraquinones																	
2	1-Cl							1678s		1572m			1319s		1267s		1236m	
3	1-OAc						1764s	1678s		1585s			1325s		1279s		1241m	1185s
4	1-OH							1667s	1631s	1582s		1357s	1290s		1266s		1230s	
5	2-Cl							1678s		1575s			1325s		1287s			
6	2-Me							1675s		1592s			1330s		1297s	1269w	1221w	
7	2-OH					3344s		1667s		1587s			1339s	1304s	1282s	1239s	1224s	
	Disubstituted anthraquinones																	
8	2-OH, 3-Me					3311s		1658s		1575s		1504m	1342s	1307s	1284w	1250s		1186s
9	2 : 3-$(OH)_2$					3472s	3268s	1675s		1585s		1520s	1340s		1289w	1245w		1193m
10	2 : 6-$(OH)_2$					3300s		1656s		1587s			1323s	1297m		1239s	1218w	
11	2 : 7-$(OMe)_2$							1672s		1590s				1305w	1284s	1241m		
12	2 : 7-$(OH)_2$						3195m	1653s		1597s				1314s	1264w			1206s
13	1-OMe, 2-Me							1669s		1572s		1325s			1277s			1198m
14	1-OH, 2-Me							1669s	1634s	1587s		1359s		1292s	1267s			1200s
15	1 : 2-$(OH)_2$					3367m		1658s	1634s	1587s		1351m	1333w		1289s			1195s
16	1 : 3-$(OH)_2$					3413s		1675m	1637s	1590s		1340s	1319s			1266m		1195w
17	1 : 4-$(OH)_2$								1626s	1582s		1355s	1314s			1256s	1220s	
18	1 : 5-$(OH)_2$								1634s	1600s	1572s			1305s		1245s	1218w	1174m
19	1 : 6-$(OH)_2$					3390m		1664s	1634s	1592s			1328w	1290w	1277m	1245m	1218w	
20	1 : 8-$(OH)_2$							1678s	1621s	1600w		1348m		1300w	1269s		1205m	
1	1163m		1098w				971m	936s					812s					693w
	Monosubstituted anthraquinones																	
2	1166s	1136m					964s		920w			831w	805s	786w	750m		702s	
3	1164m			1041m		1020m	996m				900s	862s	810s	776w	733m		708s	689m
4	1159s	1101w	1066m	1042w		1013s			927w		881s	838s	815w	775s	737m		708s	
5	1164s	1112w	1078m				965m		929s	913s	899s	857s	816m	792m			707s	
6	1164s	1147w	1083w	1043m		1008w	970s		933s		895m	850s	816w	789w			710s	
7	1175m	1145w	1088s				986s		932s	911w	883s	854s	811w	795m	749m	719s	711s	
	Disubstituted anthraquinones																	
8	1163m	1106s	1082s	1047m		1019w	963s		917m	904m	888m			797s	776s	736s	716s	693m
9	1167m	1116s	1088w	1048w	1033w	1015w	970m			903s	880w	853w	833w	794s		741w	713s	
10	1149s		1082s			1001w		934w			885s		841m		750s	732s	709m	
11		1116m	1092w		1025s		976s	930s		911s	889s	847s	822w	802m	775m		744s	712m
12			1086m		1017w			923m		901m		855s		796s		750w	735m	
13	1164s			1055s		1017m	975s	958s			882w	858s	824w		798m	755m		715s	
14	1156m			1052s		1010s					896m	850s	817w		778s	748m		710s	
15	1178s			1048m	1034w	1011s					897m	854s	829s		770s	752s		714s	
16	1163s		1098w	1063 w	1030w	1006m			923w		879w	863w		801m	778s		728m	714s	
17	1151s		1072w		1027m		981w	962s		903w	876w		838w		789s	574w			699s
18	1157s	1101w	1086s	1050s		1018w	989w				868s		824m	787s	775m			713s	
19	1156w			1065w	1037w					910w	877m	856w	827m	796m	770s	755m		713m	
20	1159m		1080m	1058m	1032m		972s		922w			846s		816s	779s	741m			

TABLE 1. (*Continued.*)

Frequencies of infrared bands

No.	Anthraquinone																	
	Trisubstituted anthraquinones																	
21	1 : 2 : 3-(OMe)$_3$								1664s		1570s			1344s	1323w	1285s	1276s	1244w	1215s	1190s
22	1 : 3-(OMe)$_2$, 2-Me								1664s		1570s			1323s		1287s			1230s	1190s
23	1 : 3-(OMe)$_2$, 2-CH$_2$·OH					3300m			1669s		1570s			1318s		1280s			1225s	1189m
24	1-OMe, 2-Me, 3-OH					3311m			1669s		1570s			1337s	1300s	1282s			1222m	1198m
25	1-OH, 2-CH$_2$·OH, 3-OMe			3521m					1658s	1629s	1572s		1504w	1339s	1300s				1230s	1188s
26	1 : 3-(OH)$_2$, 2-CH$_2$·OH			3448m	3367m				1656s	1621s	1587s	1575s		1339s	1304s	1287s		1242w	1212m	1196w
27	1 : 3-(OH)$_2$, 2-OMe				3378s				1664s	1634s	1587w	1575s		1359s		1284s	1264s		1203s	1163s
28	1 : 3-(OH)$_2$, 2-Me			3413s					1658s	1623s	1582s			1339s	1312s	1277w			1233m	1196s
29	1 : 2 : 3-(OH)$_3$				3378m				1650s	1626s	1575s			1340m	1309s	1280m	1264w		1221m	
30	1 : 2 : 4-(OH)$_3$				3226m					1621s	1580s			1337s	1309s		1264s			1183s
31	1 : 2 : 5-(OH)$_3$				3333m					1626s	1577s			1353m	1304s		1264s	1238m		1200m
32	1 : 2 : 6-(OH)$_3$				3356s	3279w		1650s			1580s				1294s			1229s		1196s
33	1 : 2 : 7-(OH)$_3$				3390w	3311s		1647s			1582s				1314s	1302s	1258w	1233w	1214w	1198s
34	1 : 2 : 8-(OH)$_3$				3378m			1661m	1621s	1570s			1506w			1290s	1266s		1209m	
35	1 : 8-(OH)$_2$, 3-Me							1675s	1621s			1558m		1350s		1287m	1271s		1208s	
36	1 : 3 : 8-(OH)$_3$				3367s			1664m	1616s	1570s				1353m		1265s		1225s		
37	1 : 4 : 8-(OH)$_3$								1605s	1575w					1321s	1282s	1259s	1221s		
	Tetrasubstituted anthraquinones																	
38	1 : 2 : 5-(OH)$_2$, 6-Me			3460m					1623s	1605m				1355m	1311w	1293s	1261w	1225s		1174m
39	1 : 2 : 5 : 8-(OMe)$_4$				3344s				1616s	1575s					1321s		1267s	1238s	1203w	
40	1 : 3 : 5 : 7-(OMe)$_4$							1653s		1595s	1555s					1304s	1256s		1214s	1193m
41	1 : 5-(OH)$_2$, 3 : 7-(OMe)$_2$								1616s	1575s				1340s		1287s	1259w		1206s	
	Trisubstituted anthraquinones																	
21	1170w	1130s	1100w	1065s	1045s	1030w	988s	962s	911s		873s	824m	802m	789s		760s		716s		
22		1134s		1068m	1021m	1006m	977s			898m	876s	826w		796m		760s		717s	686w	
23	1161m	1135s		1067s	1041m	1002s	974s			897s	873s	826m		796w		763s		717s		
24		1120s	1094w	1067m	1019m		978s		907m	887m	871w	824w		794w		762m		713s	687m	
25		1134s	1101w	1076m	1043m	1011s			924m		864s	831w		795m		756m		718s		
26	1168m	1127s		1086m	1045w	1007s	984s	955w	934w	894m	875m	824s	812s	792m		754w	738w	717s		
27		1134s	1093m	1066w	1040m	1007s	965s			896w	873s			789s		762s	735m	712s	699m	
28		1124s	1098m	1076m	1044m	1015s	973m	943m			868s	831s		804s	772w	746s	734s	713s		
29		1122s	1091w	1063w	1032s		989s				869m	834m		796m		752w		716m		
30				1064s	1029m		964s		904w		867s	831w				751s	732s	704s		
31	1160s		1087s		1032m	1013w		938m		895m	854m	834m	810m		777s	751w	735w		687s	
32			1103s		1035s	1009w	976w	959w	941w	897m	858w	847s	818w	797m	775m	752s	720s		681s	
33	1172w	1148m	1104m	1045m	1024s				942m	890m	859s		819w	800m	769w	751s	742s			
34	1160m			1073m	1029m						858s	838m	813m	792w		758w	736m		686m	
35	1160s		1086s	1052w	1024s		996w			903m	870s	841s	818w	806m		752s	733s			
36	1153s		1089m	1053m	1017s				912w	880w	864s	840s	818m	807w	774s	753s	737m		690m	
37	1157s		1093s	1057m			983s	970s		895w	853w	839m		800m	773s	745w		703m		
	Tetrasubstituted anthraquinones																	
38	1156m			1078s	1016s		968m			870w	848w			800s			734s			
39	1166s		1095s		1034w		982w	940m			845s			807m	782s	769m		711m		
40	1157s		1083m	1056s			988s	935s		869w	855s	833s		795w		761s	720s			
41	1139s		1086w	1025m			964s		903s	865m	840s						722s			

TABLE 1. (*Continued.*)

Frequencies of infrared bands.

TABLE 1. (*Continued.*)

Frequencies of infrared bands.

No.	Anthraquinone																	
										Tetrasubstituted anthraquinones							
42	1 : 3 : 5 : 7-$(OH)_4$			3344s	3077m			1608s	1580s		1497s	1326s		1282s	1242s		1199m	
43	1 : 8-$(OH)_2$, 3-OMe, 6-Me					1678m	1623s		1562s			1326s	1299s	1276s	1256m	1230s	1205w	1189w
44	1 : 3 : 8-$(OH)_3$, 6-Me			3390s		1672m	1621s		1562s			1340s	1300m	1276s	1252w	1220s		
45	1 : 3 : 8-$(OH)_3$, 6-CH_2·OH	3521m	3448s		2667m	1678m	1626s	1600s	1562s			1311s	1300s	1258s		1217s		
46	1 : 3 : 8$(OH)_3$, 6-CO_2H			3390m	3185m	1706s	1623s		1560s					1271m		1209m		
47	1 : 4 : 5-$(OH)_3$, 7-Me							1603s	1575s				1302s		1261s	1239s		1181s
48	1 : 4 : 5-$(OH)_3$, 2-Me							1592s					1312m		1245s			
49	1 : 4 : 5 : 8-$(OH)_4$							1592s	1577s						1264s		1200w	1182w
										Pentasubstituted anthraquinones							
50	1 : 2 : 3 : 5-$(OMe)_4$, 6-Me					1669s		1570s		1490m		1337s	1289s	1264s		1200s	1185s	
51	1 : 3-$(OH)_2$, 2 : 5-$(OMe)_2$, 6-Me			3300m		1653s	1629s	1562s				1340m	1284s			1198m	1174m	
52	1 : 5-$(OH)_2$, 2 : 3-$(OMe)_2$, 6-Me						1623s	1575s					1304s	1248s		1198m	1182m	
53	1 : 3 : 5-$(OH)_3$, 2-OMe, 6-Me ...			3413s			1618s	1575s				1314m	1282w	1250s		1200w	1167m	
54	1 : 2 : 3 : 5-$(OH)_4$, 6-Me		3472m		3195w		1621s	1590s			1350m	1299s	1284s		1233w	1220s	1170s	
55	1 : 2 : 3 : 7-$(OH)_4$, 6-Me	3584m 3509w	3367s		3165s		1631s	1595s		1504m	1339s	1321w		1256s	1238m			1175w
56	1 : 4 : 5 : 8-$(OH)_4$, 2-Me							1572s		1486m			1272s	1255s				1171s
57	1 : 4 : 5-$(OH)_3$, 2-Me, 7-OMe ...							1592s		1490m		1305s		1255s		1206w	1179s	
58	1 : 4 : 5 : 7-$(OH)_4$, 2-Me	3571s						1603s	1558s	1504m		1325s		1264s				1190s
59	1 : 4 : 5 : 7-$(OH)_4$, 2-CH_2·OH...			3378m			1613m	1595m	1560m					1250m				1171m
										Hexasubstituted anthraquinone							
60	1 : 2 : 3 : 5 : 6 : 7-$(OH)_6$			3367w				1645m	1582s						1263s		1198m	1183m
										Tetrasubstituted anthraquinones							
42	1148s		1085m	1014s				902s	861m	841s			806w		756m	719s	705s	
43	1163s	1139w	1105s		1035s		979s	928m	903m	875s	851s				759s*			
44	1170s		1100s		1032s		979w	943w	907s	875s	860s	829s			762s*			
45	1172s	1131w	1100s	1050s	1026s		982s	938m	914m	876s	865m	835m			759s*			
46	1170s		1104m		1025m	1000w			914w	887s					755s			
47	1164s		1105m		1033m	1002m	975w	951m	913w	879s	843s			805m	776w		739s		
48	1172s	1136w		1076s	1012s		977w		915m	890s	840m			806s	789s	752m	728s		
49	1155s						973m				838s				780s		737m		
										Pentasubstituted anthraquinones							
50	1140s		1099m	1081w	1034s	1017w	980s		936m	918s		866s	822w	802w	786w	764m	730s	709m	686w
51	1125s		1098m	1054m	1035m		988m	968m	943m	891m		853m		816s	798s	766w	744s	728m	
52	1136s		1103m	1078m	1035m		990s		957m	876w		856w		799w	784s		741m		
53	1139m		1103w	1060w	1025m		981m		949m	902w	881w	855w	833m	814m	786m	773m	738w		
54	1124s		1092m	1043m		1010s		966w		900m		854m		810m		776s			
55	1139w			1085s	1058m	1008m		972m		911w	872m	845w		812m	777w	761s	741s		
56	1134w			1079s	1026s			972s	923w	891m		849m			787s	757m	736m		
57	1159s	1136w	1089s		1021s		991m	945m	920m	909w	876s	858w	835w	823w	803s	769m	750s*		
58		1138m	1091s		1024s				921s	882s	858s				805s	771s	736s	693m	
59			1092s	1038w	1021w	1005w			923w			855w				775m		703m	
										Hexasubstituted anthraquinone							
60	1152s							972s					838s		781s		737s		

* Spectrum recorded from 2 to 14 μ only.

to the α-hydroxyl stretching frequency. To clarify the position, the spectrum of α-hydroxyanthraquinone has been re-investigated, using potassium bromide pressed discs and mulls in hexachlorobutadiene. A broad, weak absorption band with centre at approximately 2700 cm.$^{-1}$ was obtained in both cases, corresponding to the stretching frequency of chelated hydroxyl bonds.[4] In addition, there was a broad peak of medium strength at 3039 cm.$^{-1}$, assignable to the normal aryl C–H stretching frequency.

The absence in paraffin mulls of the usual hydroxyl stretching vibration is accompanied by a profound change in frequency and intensity of the stretching vibration of the carbonyl group adjacent to the α-hydroxyl group, so that a second, more intense band at lower frequency results. From his work in the hydroxyl and carbonyl regions of some hydroxy-derivatives Flett [3] suggested a useful grouping according to the arrangement of the α-hydroxyl groups in hydroxyanthraquinones, and this was extended by Howard and Raistrick [6] to include hydroxyanthraquinones with other substituted groups. With the large number of complex anthraquinones available for this study it has been possible to extend still further the usefulness of the spectra in this region. In Table 2 are set out the carbonyl frequencies of anthraquinones grouped according to the arrangement of α-hydroxy-groups on the nucleus. (The numbers in parentheses indicate the number of compounds measured.)

TABLE 2.

		C=O frequencies		
Group no.	Type of anthraquinone	*a*	*b*	Δ
1	No α-OH (18)	1678—1653	—	—
2	1-OH (14)	1675—1647	1637—1621	24—38
3	1 : 4- and 1 : 5-$(OH)_2$ (11)	1645—1608	—	—
4	1 : 8-$(OH)_2$ (8)	1678—1661	1626—1616	40—57
5	1 : 4 : 5-$(OH)_3$ (7)	1616—1592	—	—
6	1 : 4 : 5 : 8-$(OH)_4$ (2)	1592—1572	—	—

Depending on the number of carbonyl peaks and their frequency range, it is possible, with the minimum overlapping, to place an anthraquinone in one of the six groups of Table 2.

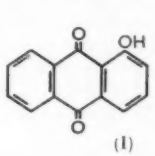
In group 3, the lone carbonyl frequency of the 1 : 3 : 5 : 7-tetrahydroxy-derivative has an exceptionally low value (1608 cm.$^{-1}$), falling below 1616 cm.$^{-1}$ which is the upper limit for the single peak of compounds in group 5. Exceptions are 1 : 2 : 6- and 1 : 2 : 7-trihydroxyanthraquinone, which, instead of the expected two carbonyl peaks, have only one, at 1650 and 1647 cm.$^{-1}$ respectively. Both 2 : 6- and 2 : 7-dihydroxyanthraquinone have very low carbonyl frequencies (1656 and 1653 cm.$^{-1}$ respectively), and it is possible that in the case of 1 : 2 : 6- and 1 : 2 : 7-trihydroxyanthraquinone, the vibrations of the two carbonyl groups, now that they are closer in frequency and linked through a conjugated system, have become indistinguishable. In the case of 1 : 2 : 3 : 7-tetrahydroxy-6-methylanthraquinone (compound 55), the weaker of the two carbonyl absorptions (normally expected to appear at about 1675 cm.$^{-1}$) is masked by the strong, very broad peak at 1595 cm.$^{-1}$, while the stronger carbonyl absorption appears only as a band on the side of the 1595 cm.$^{-1}$ peak. Another apparent exception is 1 : 3 : 8-trihydroxyanthraquinone-6-carboxylic acid (compound 46) where the high-frequency carbonyl band is masked by the absorption of the carboxyl group at 1706 cm.$^{-1}$.

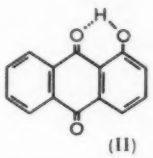
In anthraquinones with no α-hydroxyl groups, the single carbonyl frequency occurs between 1678 and 1653 cm.$^{-1}$ and, except in cases of strongly electrophilic substituent groups which raise the frequency a few cm.$^{-1}$, the position and nature of the substituent groups have no noticeable effect on the carbonyl frequency. This is in contrast with the benzoquinones, where the effect of substituent groups can be predicted.[7]

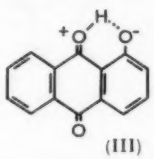
The lowered frequency of the α-hydroxyl group and the accompanying changes of intensity and frequency in the carbonyl region have been ascribed by Hilbert, Wulf, Hendricks, and Liddel [8] to what was later called " conjugated-chelation " [8] where the strength of hydrogen-bonding between the hydroxyl and the carbonyl group (I) and (II) is enhanced by resonance with an ionic form (III) having a conjugated system in which the donor-acceptor properties of the chelating centres are increased. A conjugated-chelate system always results in the disappearance or lowering of the hydroxyl stretching frequency, and at the same time the

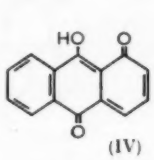
[6] Howard and Raistrick, *Biochem. J.*, 1955, **59**, 478.
[7] Yates, Ardao, and Fieser, *J. Amer. Chem. Soc.*, 1956, **78**, 650.
[8] Rasmussen, Tunnicliff, and Brattain, *ibid.*, 1949, **71**, 1068.

carbonyl band is lowered in frequency and increased in intensity owing to the weakened force constant and increased moment of the bond. Flett [3] considers an ionic form unimportant, but considers that form (IV) makes a considerable contribution. Josien, Fuson, Lebas, and Gregory [9] consider the hydrogen to be equally bonded to the two oxygen atoms in a similar way, but Hadži and Sheppard [8] reject these suggestions since too great a lowering of the hydroxyl frequency would result. They also suggest considerable resonance through the conjugated system (II) and (III). Further consideration, however, as, for example, a comparison of α- and β-hydroxy- and α- and β-amino-anthraquinone, suggests that the primary cause of the lowering of the carbonyl frequency of α-hydroxyanthraquinones is, not chelation, but altered electron-distribution as in forms (V)–(VI) and (VII)–(VIII), chelation serving only to stabilize the resulting ionic forms.


(I)


(II)


(III)

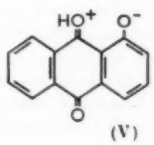

(IV)

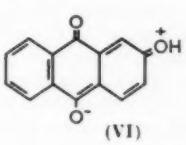
Electron re-distribution to give an ionic form $=OH^+$ takes place less readily than that giving $=NH_2^+$ in the amino-derivatives, and this is reflected in the frequencies of the perturbed carbonyl vibrations of α- and β-aminoanthraquinone [3] compared with the frequencies of the corresponding hydroxyanthraquinones set out in Table 3. Chelation is not important for aminoanthra-

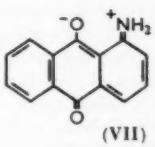
TABLE 3.

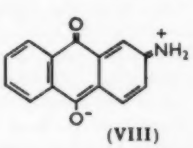
Anthraquinone	C=O frequencies *a*	*b*	Hydrogen-stretching frequencies
Anthraquinone	1675	—	—
α-Amino	1665	1612	3420, 3300
β-Amino	1676	1625	3470, 3330, 3220
α-Hydroxy	1667	1631	—
β-Hydroxy	1667	—	3344

quinones, hydrogen stretching frequencies in the α- and β-substituted compounds being hardly different. That the single carbonyl frequency of β-hydroxyanthraquinone is lower than that of anthraquinone itself suggests a small contribution from the mesomeric effect, as in (VI).


(V)


(VI)

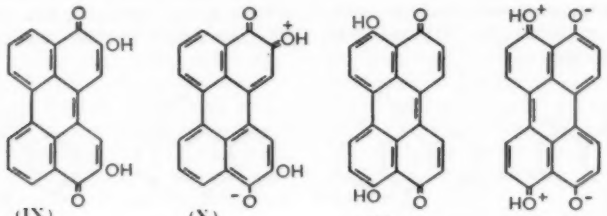

(VII)


(VIII)

In the same way the carbonyl frequency of α-hydroxyanthraquinone is initially lowered by resonance with an ionic form (V), which is stabilised by chelation because of the greater donor-acceptor properties of the ionic forms of the carbonyl and hydroxyl groups (III). That chelation, of itself, does not lower the carbonyl frequency is shown by the extended quinones, 2 : 11- (IX) and 4 : 9-dihydroxyperylene-3 : 10-quinone (XI), where the carbonyl vibrations absorb at 1621 cm.$^{-1}$ and 1631 cm.$^{-1}$ respectively,[10, 11] even though hydrogen bonding is so strong in the second compound that it has no hydroxyl absorption peak. In spite of the fact that chelation through a five-membered ring, of either the ionic (X) or the non-ionic form (IX) of the first compound, is less likely than chelation of the two forms (XI) and (XII) of the second compound, the carbonyl frequency of the first compound is the lower. This suggests, as in the case with the aminoanthraquinones, that altered electron distribution, rather than chelation, is primarily responsible for the lowering of the carbonyl frequency of hydroxy-quinones.

[9] Josien, Fuson, Lebas, and Gregory, *J. Chem. Phys.*, 1953, **21**, 331.
[10] Brown and Todd, *J.*, 1954, 1280.
[11] Calderbank, Johnson, and Todd, *J.*, 1954, 1285.

All the compounds examined have a further strong band in the double-bond region characteristic of C=C frequency. The position of this varies, but is most often around 1575 cm.$^{-1}$. In a few cases where the carbonyl frequency is very low, the two bands are indistinguishable. A similar band in the spectra of the *p*-benzoquinones at a slightly higher frequency [7] is attributed to the C=C stretching frequency of the quinone. For anthraquinones the double bonds that are conjugated directly with a carbonyl vibration have a more aromatic nature and occur at a lower frequency than normal. Further aromatic absorption occurs less



regularly throughout the series, but is often masked by peaks of the mulling agent. The band around 1575 cm.$^{-1}$ is useful in distinguishing anthraquinones of the 1 : 4- and the 1 : 5-dihydroxy-group from those of the 1 : 4 : 5-trihydroxy-group. Both groups have only one carbonyl absorption band, and the frequency range in the two cases overlaps. The C=C peak has a frequency greater than 1575 cm.$^{-1}$ characteristic of the 1 : 4- and 1 : 5-dihydroxy-group of anthraquinones, but less than 1575 cm.$^{-1}$ of the 1 : 4 : 5-trihydroxy-group. If there appears to be more than one such peak, the average frequency of peaks higher than 1500 cm.$^{-1}$ is taken for classification. For anthraquinones in the 1 : 4 : 5 : 8-tetrahydroxy-group the C=O and C=C frequencies are indistinguishable. For anthraquinones having no α-hydroxyl groups the C=C band generally has a higher frequency and is less variable than in the other groups.

It is not possible to assign further peaks to particular vibrations. Hadži and Sheppard [5] assigned some bands in the spectra of four hydroxyanthraquinones to hydroxyl deformation vibrations, but similar bands are found in most anthraquinones, whether containing hydroxyl groups or not. The out-of-plane C–H deformation bands are expected to be found in the region 900—650 cm.$^{-1}$. Absorption bands of methyl and methylene substituent groups are obscured by the mulling agent.

Apart from the regions of their characteristic absorption the effect of substituent groups on the rest of the spectrum is small, the position of a group on the anthraquinone nucleus being of more importance in determining the overall spectrum than the nature of the group. This is so, not only in the region of the C–H out-of-plane deformation vibrations of the anthraquinone nucleus where substitution of another group for a hydrogen atom must change the vibration spectrum, but also from the double-bond stretching region down through the C–H deformation vibrations beginning around 900 cm.$^{-1}$.

It may be seen from Table 1, that derivatives listed under the same heading of substitution pattern have many common bands within a narrow range of frequency and intensity. There are eleven groups of anthraquinones with different characteristic substitution patterns. Perusal of the Table shows that the common bands in each group can be distinguished from those of other groups, thus enabling an unknown anthraquinone to be classified within a definite group and therefore assisting in its identification (with the help of other available chemical, physical, and biosynthetic evidence).

Summary of Diagnostic Features.—(1) The infrared absorption spectrum of each of the 60 anthraquinones is unique and can be used to " fingerprint " each compound.

(2) β-Hydroxyl groups can be detected by the appearance of a sharp band in the region 3600—3150 cm.$^{-1}$. If there is more than one such band, two or more hydroxyl groups are attached to the anthraquinone nucleus in β-positions, each having a different environment.

(3) Derivatives with no α-hydroxyl group have one strong carbonyl band in the region 1678—1653 cm.$^{-1}$.

(4) Derivatives with one α-hydroxyl group have two carbonyl frequencies, one in the region

1675—1647 cm.$^{-1}$, and an even stronger band between 1637 and 1621 cm.$^{-1}$, the frequency separation between the bands lying in the range 24—38 cm.$^{-1}$.

(5) Substitution by two α-hydroxyl groups in the 1 : 4- and 1 : 5-positions yields spectra with a single carbonyl band between 1645 and 1608 cm.$^{-1}$.

(6) Derivatives with two α-hydroxyl groups in the 1 : 8-positions have two bands, one between 1678 and 1661 cm.$^{-1}$ and the other, stronger one between 1626 and 1616 cm.$^{-1}$, the frequency separation between the peaks lying between 40 and 57 cm.$^{-1}$.

(7) Substitution of α-hydroxyl groups in the 1 : 4 : 5-positions yields a single carbonyl band between 1616 and 1592 cm.$^{-1}$.

(8) Derivatives with four α-hydroxyl groups, *i.e.*, in the 1 : 4 : 5 : 8-positions, have a single carbonyl band, in the region 1592—1572 cm.$^{-1}$.

(9) The average C=C stretching band in anthraquinones of the 1 : 4- and the 1 : 5-dihydroxy-group has a frequency greater than 1575 cm.$^{-1}$, while in the case of the 1 : 4 : 5-trihydroxy-group, it is less than 1575 cm.$^{-1}$. For anthraquinones of the 1 : 4 : 5 : 8-tetrahydroxy-group, the C=O and C=C bands are indistinguishable.

(10) It is possible to group the spectra of anthraquinones of the same substitution pattern according to the frequency and intensity of the absorption bands.

We thank Professor H. Raistrick, Sir Robert Robinson, O.M., F.R.S., Dr. B. Siegfried, Imperial Chemical Industries Limited, and CIBA Ltd., for many compounds used in this investigation. We are grateful to Messrs. R. N. Seelye and L. Colebrook for helpful discussion and assistance in checking the Tables. Assistance is also gratefully acknowledged from the Chemical Society, the Rockefeller Foundation of New York, the Australian and New Zealand Association for the Advancement of Science, and the Research Grants Committee of the University of New Zealand. One author (B. C.) is further indebted for a University Research Fund Fellowship.

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Auckland, New Zealand. [*Received, August 15th*, 1958.]

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34. *Pyrroles and Related Compounds. Part II.* Michael Addition to Pyrromethenes.*

By A. C. Jain and G. W. Kenner.

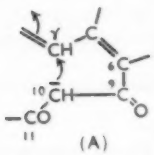
In connection with a speculation about the biosynthesis of chlorophyll, the Michael addition of cyanoacetic ester to pyrromethenes (I) has been studied. Usually the adduct (II) is degraded to the ethyl α-cyano-β-2-pyrrolylacrylate (III), but its general structure is preserved in one product (IV; X = CN).

Fischer commented on the close structural relation between chlorophyll *a* and hæmin; apart from the presence of magnesium and the esterifying phytyl and methyl residues in chlorophyll *a*, it differs from hæmin in possessing (1) two hydrogen atoms at positions 7 and 8, being a chlorin, (2) a carbonyl group at position 9, (3) an isocyclic ring, and (4) an ethyl, instead of a vinyl, group at position 4. Regarding hæmin as the biologically more fundamental pigment, he envisaged the following formal transformations of protoporphyrin IX:[1] " Oxydiert man die in 6-Stellung befindliche Propionsäure in β-Stellung zur Ketopropionsäure, versetzt die beiden Wasserstoffatome von 9 an Stellung 7 und 8, führt dehydrierenden Ringschluss von C-10 zur γ-Methinbrücke aus und verlagert diese beiden Wasserstoffatome an die Vinylgruppe in 2 (*sic*), so entsteht die Formel für Phäophorbid *a*." Meantime the common origin of the two pigments from porphobilinogen

* Part I, *J.*, 1958, 3779. Some of the material in the present paper was presented to the XVIth International Congress of Pure and Applied Chemistry, Paris, 1957.

[1] Fischer and Stern, " Chemie des Pyrrols," Akademische Verlag, Leipzig, 1940, Vol. II, Part 2, pp. 37—38.

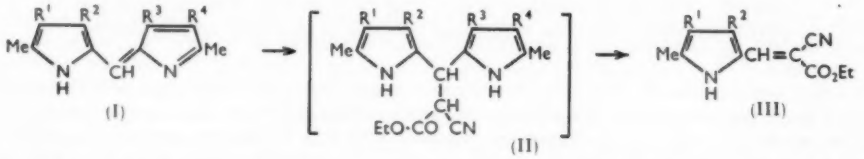
and protoporphyrin has been established experimentally.[2] The route from protoporphyrin to chlorophyll *a* is believed to pass through magnesium 2-vinylphæoporphyrin-a_5,[3] which already possesses structural features (2), (3), and (4) as well as the esterifying methyl group. Probably feature (1) and the phytyl group are added successively after this stage.[4] As to the steps preceding it, β-oxidation of the propionic acid side-chain, covering feature (2), has a reasonable analogy in the aliphatic series, and it has been advanced [5] as a plausible mechanism for the decarboxylation of the side-chains, which appear as vinyl groups in protoporphyrin, at positions 2 and 4 in uroporphyrin III. We now suggest that either the methyl ester or the coenzyme A derivative of this keto-acid would be disposed, when ionised or enolised, towards closure of the isocyclic ring by a change of the Michael type (A).



(A)

The electrons displaced from the γ-methine group would have to be accepted by either an oxidising agent or a conjugated double bond, as in the ordinary Michael reaction. If the biochemical evidence that saturation of the 7 : 8-double bond takes place independently is accepted, it is tempting to follow Fischer's formal scheme connecting saturation of the vinyl group with closure of the isocyclic ring. However this may be, it is in our opinion worthwhile striving to prepare the appropriate β-keto-acid derivatives for both chemical and biochemical studies. As a preliminary task, the reactivity of the more accessible pyrromethenes has been studied, since they can be regarded as crude models of half the porphyrin molecule or rather its magnesium complex, which is more probably involved in the cyclisation.

The behaviour of the readily accessible 4 : 4′-diethyl-3 : 5 : 3′ : 5′-tetramethylpyrromethene (I; $R^1 = R^4 = Et$, $R^2 = R^3 = Me$) with malonic, acetoacetic, and cyanoacetic esters under the usual conditions of Michael reactions was examined. Only cyanoacetic ester was sufficiently reactive and, whether basic or acidic catalysis was used, the isolated product was a yellow crystalline substance, identical with a synthetic sample of ethyl α-cyano-β-(4-ethyl-3 : 5-dimethyl-2-pyrrolyl)acrylate (III; $R^1 = Et$, $R^2 = Me$). Mechanisms in accordance with the usual electronic theory can easily be written to account for formation of an adduct (II) and its decomposition to the yellow product (III); under acidic conditions the pyrromethene would be in the more reactive form of its hydrochloride. Moreover, there are numerous analogies for decomposition of the hypothetical adduct with ejection of a pyrrole residue.[6] It is likely that some of the colourless adduct (II) was present in the substantial uncrystallised residue from the reaction under basic catalysis, but most of the material from the acidic reaction was accounted for as recovered starting



(I) (II) (III)

material or the yellow product. A similar yellow compound (III; $R^1 = Me$, $R^2 = H$) was obtained likewise from an unsymmetrical pyrromethene (I; $R^1 = R^3 = Me$, $R^2 = H$, $R^4 = Et$). As the fragment eliminated here from the presumed intermediate

[2] Rimington, *Ann. Rev. Biochem.*, 1957, **26**, 572.

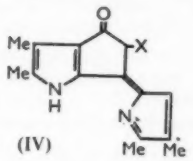
[3] Granick, "Chemical Pathways of Metabolism" (ed. Greenberg), Academic Press, New York, 1954, Vol. II, p. 287; "Porphyrin Biosynthesis and Metabolism" (ed. Wolstenholme and Millar), Churchill, London, 1955, p. 143.

[4] Wolff and Price, *Arch. Biochem. Biophys.*, 1957, **72**, 293.

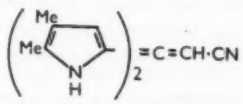
[5] MacDonald, "Porphyrin Biosynthesis and Metabolism" (ed. Wolstenholme and Millar), Churchill, London, 1955, p. 155.

[6] *E.g.*, Fischer and Ammann, *Ber.*, 1923, **56**, 2319; Corwin and Andrews, *J. Amer. Chem. Soc.*, 1936, **58**, 1086; 1937, **59**, 1973; Paden, Corwin, and Bailey, *ibid.*, 1940, **62**, 418; Treibs, Herrmann, Meissner, and Kuhn, *Annalen*, 1957, **602**, 153.

(II; $R^1 = R^3 = Me$, $R^2 = H$, $R^4 = Et$) was 3-ethyl-2 : 4-dimethylpyrrole, just as in the former instance, it seemed that decomposition of the adduct might have been encouraged by substituents in the 4- and the 4′-position, and therefore the adduct (II; $R^1 = R^4 = Me$, $R^2 = R^3 = H$) might actually be obtained from another symmetrical pyrromethene (I; $R^1 = R^4 = Me$, $R^2 = R^3 = H$). However, once more the decomposition product (III; $R^1 = Me$, $R^2 = H$), identical with that from the unsymmetrical pyrromethene, was produced under both basic and acidic conditions, but from the former reaction a second, red crystalline product was isolated. Apparently this substance, to which we assign structure (IV; X = CN), arises from the adduct (II; $R^1 = R^4 = Me$, $R^2 = R^3 = H$) through condensation between the ester group and the neighbouring free β-position and dehydrogenation by another molecule of pyrromethene. Its absorption of visible and ultraviolet light resembles that of pyrromethenes, for example the starting material (I; $R^1 = R^4 = Me$, $R^2 = R^3 = H$), while the infrared spectrum shows in addition bands at 2200 and 1713 cm.$^{-1}$ corresponding to the nitrile and the cyclic carbonyl group. The expected position of the latter can only be conjectured, the opposing influences of ring-strain and of conjugation with the pyrrole nucleus being borne in mind, but it is noteworthy that absorption by chlorophyll derivatives at 1700 cm.$^{-1}$ has been ascribed to the rather similarly situated cyclic carbonyl group.[7] Attack on the nitrile group appeared to be hindered sterically, but the amide (IV; X = CO·NH$_2$) was formed by warm 85%



(IV)



(V)

sulphuric acid and its absorption spectra confirmed the structure (IV). Alkaline hydrolysis of the nitrile removed the carbonyl group, producing a yellow crystalline material. Although we lack a sample synthesised by another route for comparison because di-(4 : 5-dimethyl-2-pyrrolyl) ketone does not have normal carbonyl properties (cf. spectral data in Experimental section), we regard structure (V) as justified by the analytical and spectral data and as supporting the assignment of structure (IV; X = CN) to the precursor.

Viewed in the broadest way, our results merely extend the published evidence, provided especially by the work of Corwin and his colleagues,[6,8] that the methine bridge of pyrromethenes has considerable cationoid reactivity, but we think that they make the hypothesis expounded in the first paragraph more plausible by providing closer analogies. Still better would be studies of pyrromethenes bearing the β-diketo-side-chain, but we have not yet succeeded in preparing such compounds. Studies in the porphyrin series are in progress.

Experimental

Ethyl α-Cyano-β-(4-ethyl-3 : 5-dimethyl-2-pyrrolyl)acrylate (III; $R^1 = Et$, $R^2 = Me$).—3-Ethyl-5-formyl-2 : 4-dimethylpyrrole was conveniently prepared in 90% yield from 3-ethyl-2 : 4-dimethylpyrrole by the phosphoryl chloride–dimethylformamide reaction.[9] A solution of the aldehyde (1·5 g.), ethyl cyanoacetate (1·1 c.c.), ammonium acetate (0·2 g.), and glacial acetic acid (0·1 c.c.) in benzene was boiled vigorously during 3 hr. while water was drawn off through a Vigreux fractionating column fitted with a Dean–Stark head.[10] The residue from evaporation of the benzene was extracted with boiling *n*-hexane which, on being cooled, deposited lemon-yellow needles (1·4 g.) of the product, m. p. 123—124° (ref. 11 records m. p.

[7] Weigl and Livingston, *J. Amer. Chem. Soc.*, 1953, **75**, 2173.
[8] Brunings and Corwin, *ibid.*, 1944, **66**, 337; Corwin and Doak, *ibid.*, 1955, **77**, 464.
[9] Chu and Chu, *J. Org. Chem.*, 1954, **19**, 266; Smith, *J.*, 1954, 3845.
[10] Cf. Cope, Hofmann, Wyckoff, and Hardenbergh, *J. Amer. Chem. Soc.*, 1941, **63**, 3453.
[11] Fischer and Neber, *Annalen*, 1932, **496**, 12.

121°), absorption maxima in ethanolic solution at 309, 403 mμ (log ε 3·58, 4·64 respectively) and in Nujol mull at 2215, 1710, 1595, 1550 cm.$^{-1}$.

Ethyl α-Cyano-β-(4 : 5-dimethyl-2-pyrrolyl)acrylate (III; R^1 = Me, R^2 = H).—2 : 3-Dimethylpyrrole was prepared by the published method,[12] except that hydrolysis and decarboxylation were carried out separately in boiling dilute sodium hydroxide solution (4 hr.) and in 2-aminoethanol at 160° (1 hr.), and it was converted into 2-formyl-4 : 5-dimethylpyrrole by the phosphoryl chloride–dimethylformamide reaction[9] (75% yield). Condensation of the aldehyde and ethyl cyanoacetate, as in the foregoing preparation, afforded small needles, m. p. 184—185°, of the *product* (Found: C, 66·0; H, 6·5; N, 13·0. $C_{12}H_{14}O_2N_2$ requires C, 66·0; H, 6·5; N, 12·8%), absorption maxima in ethanolic solution at 213, 293, 405 mμ (log ε 3·88, 3·01, 4·71 respectively) and in Nujol mull at 2190, 1700, 1590, 1552 cm.$^{-1}$.

Reactions between 4 : 4′-Diethyl-3 : 5 : 3′ : 5′-tetramethylpyrromethene (I; R^1 = R^4 = Et, R^2 = R^3 = Me) *and Ethyl Cyanoacetate.*—3-Ethyl-2 : 4-dimethylpyrrole was prepared from ethyl 4-acetyl-3 : 5-dimethylpyrrole-2-carboxylate in 80—85% yield by successive hydrogenation with Raney nickel catalyst,[13] alkaline hydrolysis, and acidic decarboxylation in preference to the previously recommended single operation.[14] The derived pyrromethene,[15] m. p. 148—149°, showed absorption maxima in ethanolic solution at 225, 328, 447 mμ (log ε 4·01, 3·53, 4·55 respectively).

A solution of the pyrromethene (1 g.) in freshly distilled ethyl cyanoacetate (5 c.c.) was heated with triethylamine (0·3 c.c.) at 100—105° during 2 hr. The residue from evaporation of the excess of ester under reduced pressure was extracted with boiling light petroleum (b. p. 60—80°), which left a dark tar. When the extract was percolated through a column of animal charcoal, concentrated, and cooled, it deposited ethyl α-cyano-β-(4-ethyl-3 : 5-dimethyl-2-pyrrolyl)acrylate (0·2 g.), identical with material prepared by the previously described method.

A similar experiment, in which the initial solution was saturated with dry hydrogen chloride and triethylamine was omitted, yielded the same product (0·1 g.), and starting material was recovered from the extracted residue by dissolution in ethanol and neutralisation with a few drops of aqueous ammonia solution.

Reactions between 4-Ethyl-3 : 5-4′ : 5′-tetramethylpyrromethene (I; R^1 = R^4 = Me, R^2 = H, R^4 = Et) *and Ethyl Cyanoacetate.*—The hydrobromide of the pyrromethene was prepared by Heidelmann's route,[16] and it was converted into the free base, m. p. 300° (decomp.), by shaking its solution in chloroform with lime water. The reaction with ethyl cyanoacetate and triethylamine, carried out as in the foregoing example, yielded ethyl α-cyano-β-(4 : 5-dimethyl-2-pyrrolyl)-acrylate (0·18 g.), identical with material prepared by the previously described method. The same product (0·085 g.) was obtained by acidic catalysis of the reaction.

Reactions between 4 : 5 : 4′ : 5′-Tetramethylpyrromethene and Ethyl Cyanoacetate.—The pyrromethene,[13] m. p. 115—116°, showed absorption maxima in solution in dioxan at 223, 308, 438 mμ (log ε 3·98, 3·65, 4·47 respectively) and in Nujol mull at 3480—3300 w, 1620 s, 1565 cm.$^{-1}$. Its acid-catalysed reaction with ethyl cyanoacetate yielded ethyl α-cyano-β-(4 : 5-dimethyl-2-pyrrolyl)acrylate (0·10 g.) as in the foregoing experiments.

A mixture of the pyrromethene (1 g.), triethylamine (0·35 c.c.), and ethyl cyanoacetate (5 c.c.) was kept between 100° and 105° during 2 hr.; red crystals began to separate after 1 hr. The usual procedure then furnished 0·15 g. of the same yellow product as obtained by acidic catalysis. The red crystalline residue (0·1 g.) from the extraction with light petroleum was recrystallised from ethyl acetate and sublimed at 220—230°/0·01 mm. in clusters of red needles, m. p. 279—280°; this cyano-ketone {*5-cyano-6-(4 : 5-dimethyl-2H-pyrrolylidene)-1 : 4 : 5 : 6-tetrahydro-2 : 3-dimethyl-4-oxocyclopenta*[b]*pyrrole*} (IV; X = CN) (Found: C, 72·1; H, 5·6; N, 15·8. $C_{16}H_{15}ON_3$ requires C, 72·4; H, 5·7; N, 15·8%) showed absorption maxima in ethanolic solution at 242, 318, 445 mμ (log ε 4·00, 3·90, 4·61 respectively) and in Nujol or hexachlorobutadiene mulls at 3310 s, 3100 w, 2930 w, 2860 w, 2200 s, 1713 s, 1598 s, 1515 s, 1463 w, 1363, 1337 w, 1272 s, 1245, 1222, 1157, 1067, 1020 w, 975, 854, 800, 752 s, 716 cm.$^{-1}$.

This cyano-ketone (IV; X = CN) was recovered unchanged from attempted reactions with concentrated hydrochloric acid diluted with 2 vols. of ethanol (2 hr. at 100°) and with hydrogen

[12] Corwin and Krieble, *J. Amer. Chem. Soc.*, 1941, **63**, 1831.
[13] Signaigo and Adkins, *ibid.*, 1936, **58**, 710.
[14] Fischer, *Org. Synth.*, 1941, **21**, 67.
[15] Fischer, Halbig, and Walach, *Annalen*, 1927, **452**, 297.
[16] Fischer and Orth, "Chemie des Pyrrols," Akademische Verlag, Leipzig, 1937, Vol. II, Part 1, p. 13.

chloride in dioxan (30 hr. at 20° and 4 hr. at 100°). A solution of the cyano-ketone (0·10 g.) in 85% sulphuric acid (2 c.c.) was kept between 80° and 90° during 1 hr. before being poured on ice. Ethereal extraction of the aqueous mixture afforded the *amide* (IV; X = $CO{\cdot}NH_2$) (0·02 g.), which was sublimed at 220—230°/0·01 mm. in red prisms, m. p. 263—264° (Found: C, 67·8; H, 6·2; N, 14·5. $C_{16}H_{17}O_2N_3$ requires C, 67·8; H, 6·1; N, 14·8%), showing absorption maxima in ethanolic solution at 257, 316, 452 mμ (log ε 4·12, 3·89, 4·53 respectively) and in Nujol or hexachlorobutadiene mulls at 3390 s, 3200 s, 2930 w, 1690 s, 1647 s, 1610, 1600, 1522, 1505, 1450 s, 1373 w, 1337, 1302 s, 1276 s, 1237, 1219 w, 1182, 1063, 1009, 975, 915 w, 865, 797 s, 752 w, 720 w cm.$^{-1}$.

A solution of the cyano-ketone (IV; X = CN) (0·20 g.) in alcohol (300 c.c.) was boiled during 2 hr. with 20% aqueous sodium hydroxide solution (15 c.c.); evolution of ammonia was not detected. On concentration under reduced pressure the solution deposited crude ββ-*di*-(4 : 5-*dimethyl*-2-*pyrrolyl*)*acrylonitrile* (V) (0·18 g.) which recrystallised from ether–*n*-hexane in pale yellow prisms, m. p. 167—168° (Found: C, 74·9; H, 7·1; N, 17·0. $C_{15}H_{17}N_3$ requires C, 75·3; H, 7·2; N, 17·6%), showing absorption maxima in dioxan solution at 355 mμ (log ε 4·50) and in Nujol or hexachlorobutadiene mulls at 3390, 3320 s, 2930, 2190 s, 1547 s, 1500 s, 1470 w, 1289, 1267, 1195, 1155, 1017 w, 970 w, 855 w, 807, 745 cm.$^{-1}$.

Di-(4 : 5-*dimethyl*-2-*pyrrolyl*) *Ketone*.—Prepared according to ref. 17, this compound showed absorption maxima in ethanolic solution at 256, 369 mμ (log ε 3·92, 4·52 respectively) and in Nujol or hexachlorobutadiene mulls at 3200 s broad, 2915, 2860, 2790 w, 1580, 1515 s, 1461, 1390, 1377, 1369, 1345, 1265 s, 1184 s, 1044, 970, 860 s, 827, 805 w, 758, 706 cm.$^{-1}$; these spectra are consistent with a tautomeric hydroxypyrromethene structure. Attempts to condense the compound with either ethyl cyanoacetate or cyanoacetic acid were unsuccessful.

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[17] Fischer and Orth, *Annalen*, 1933, **502**, 251.

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35. *The Preparation and Rearrangement of Benzoates and Substituted Benzoates of Dibromopropanols.*

By J. H. C. NAYLER.

Pure crystalline benzoates of 2 : 3-dibromopropan-1-ol and 1 : 3-dibromopropan-2-ol have been prepared: above 100° they partially rearrange to an oily mixture of the two. The liquids which previous investigators have described as pure must have been such mixtures. Various substituted benzoates of the dibromopropanols have been prepared, and the thermal rearrangement of some of them studied. Esters of the weaker aromatic acids rearrange more easily than those of the stronger acids. Although allyl esters of strong aromatic acids gave pure 2 : 3-dibromopropyl esters when treated with bromine in chloroform at room temperature, the corresponding esters of weaker acids gave mixed esters. Reaction mechanisms are discussed.

ACCOUNTS of the benzoates of 2 : 3-dibromopropan-1-ol and 1 : 3-dibromopropan-2-ol, which were required for another investigation, are unsatisfactory. Philippi and Seka [1] claimed to have prepared the former ester by heating 2 : 3-dibromopropanol with benzoyl chloride, and Hurd and Pilgrim [2] reported the similar preparation of the latter from 1 : 3-dibromopropan-2-ol. Edwards and Hodges,[3] however, found that the liquid products of these two syntheses had identical boiling points and infrared absorption spectra, whilst catalytic dehalogenation of either gave *n*-propyl benzoate. They concluded that both products were 2 : 3-dibromopropyl benzoate, which in one case was supposedly formed by

[1] Philippi and Seka, *Annalen*, 1923, **433**, 88.
[2] Hurd and Pilgrim, *J. Amer. Chem. Soc.*, 1933, **55**, 1195.
[3] Edwards and Hodges, *J.*, 1953, 3427.

rapid rearrangement of the isomer or an intermediate complex, although no rigorous proof of the absence of the 1 : 3-dibromo-derivative was offered. On the basis of similar evidence they later formulated the liquid adduct from allyl bromide and benzoyl hypobromite as 2 : 3-dibromopropyl benzoate.[4] Yasnopolsky's claim [5] to have prepared 2 : 3-dibromopropyl benzoate, m. p. 86—88°, in poor yield by reaction of 2 : 3-dibromopropan-1-ol with benzoyl chloride in the presence of strong aqueous sodium hydroxide was not supported by analytical evidence and could not be substantiated in this laboratory.

It has now been found that both 2 : 3-dibromopropan-1-ol and 1 : 3-dibromopropan-2-ol can be esterified by heating them with benzoyl chloride without appreciable rearrangement provided excessively high temperatures are avoided. In each case equimolecular proportions of the reagents were heated together on the steam-bath until evolution of hydrogen chloride ceased, and the product was purified by crystallisation from methanol. Alternatively, heating could be avoided completely by carrying out the initial reactions at 0° in the presence of pyridine. Good yields were obtained by both routes. The melting point of 2 : 3-dibromopropyl benzoate was 33—34° and that of the isomer 32—33°: admixture of the isomers at room temperature caused liquefaction. When warmed with sodium iodide in acetone 2 : 3-dibromopropyl benzoate, in common with other vicinal dibromides,[6] caused iodine to be liberated, but the isomeric benzoate did not. Finally, the infrared absorption spectra of the two isomeric benzoates were distinctive (see p. 193).

Neither benzoate could be purified by distillation. When either crude ester, prepared in the presence or absence of pyridine, was distilled the product was a colourless oil, b. p. 120°/0·4 mm., which afforded correct analytical data but did not crystallise. The infrared spectra showed they were mixtures. Apparently either ester undergoes partial rearrangement to a mixture of the two when heated somewhat above 100°, so the liquids prepared by earlier investigators must have been such mixtures. In Philippi and Seka's preparation [1] the temperature of the initial reaction was high enough to cause isomerisation, but presumably later workers [2,3] would have obtained pure esters if they had isolated their products by crystallisation instead of distillation. Of the five absorption bands regarded by Edwards and Hodges [3] as characteristic of 2 : 3-dibromopropyl benzoate, that at 11·9 μ is actually characteristic of its isomer, those at 7·05, 8·5, and 9·75 μ are common to the spectra of both isomers, and that at 9·5 μ is shown by neither pure ester.

The remarkable ease with which the two benzoates undergo reversible thermal isomerisation made it desirable to confirm the spectral evidence by isolating the rearrangement products. Unfortunately, the isomeric benzoates would be difficult to separate because they have very similar solubilities in the common organic solvents, whilst distillation is of course precluded. In the hope of obtaining more readily separable isomers, sixteen substituted benzoates, of which twelve were new, were synthesised from the acid chlorides and the dibromopropanols at 0° in the presence of pyridine. Most of them could doubtless also be prepared by heating the reactants in the absence of a base at moderate temperatures: indeed 2 : 3-dibromopropyl *p*-cyanobenzoate has been prepared previously in this way.[7] As with the unsubstituted benzoates, only the 2 : 3-dibromopropyl esters liberated iodine when warmed with sodium iodide in acetone. (When testing nitrobenzoates in this way it was necessary to add water so as to destroy the coloured complexes which aromatic nitro-compounds give with sodium iodide in acetone [8] before the presence or absence of iodine could be observed.) The dibromopropyl *p*-anisates, *p*-chlorobenzoates, and 3 : 5-dinitrobenzoates were chosen for thermal isomerisation studies because of favourable solubility relations and distinctive melting points.

When solutions of 2 : 3-dibromopropyl *p*-anisate and its isomer in toluene were each refluxed for 24 hours isomerisation occurred to a small extent, the products being separated

[4] Edwards and Hodges, *J.*, 1954, 761.
[5] Yasnopolsky, *J. Gen. Chem. U.S.S.R.*; 1954, **24**, 2033 (U.S. transln.).
[6] Finkelstein, *Ber.*, 1910, **43**, 1530.
[7] Chow and Gisvold, *J. Amer. Pharm. Assoc.*, 1952, **41**, 202.
[8] Shellman, *J. Org. Chem.*, 1957, **22**, 818; Blatt and Gross, *ibid.*, p. 1046.

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by fractional crystallisation from methanol. A similar period of refluxing in xylene caused more extensive isomerisation, either pure anisate giving an equilibrium mixture from which about equal amounts of the two isomers were isolated. Since rearrangement proceeded equally well in the presence of calcium carbonate, it appeared to be truly thermal and not to require catalysis by acidic decomposition products.

The *p*-chlorobenzoates were somewhat less labile (unchanged in boiling toluene for 24 hours). In boiling xylene there was appreciable rearrangement, the equilibrium mixture, again containing about equal proportions of the isomers, being obtained after 72 hours. Isomerisation in boiling acetic acid was also examined because this solvent was a convenient one in which to prepare bisthiuronium salts from dibromo-esters:[9] considerable rearrangement was detected but side-reactions probably also occurred since the total recovery of crystalline material was rather poor.

Thermal isomerisation of the two 3 : 5-dinitrobenzoates could not be demonstrated: they were recovered after 24 hours' refluxing in either xylene or anisole, whilst in boiling *p*-cymene or nitrobenzene gross decomposition ensued.

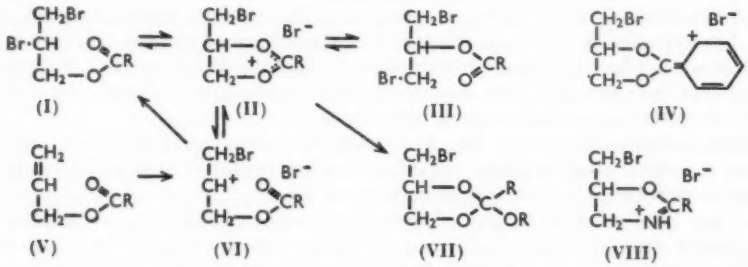
There has been no opportunity to extend these thermal isomerisation studies to the dibromopropyl esters of aliphatic acids, but certain deductions can be drawn from published data. The retention of optical activity during the preparation of the propionate, hexanoate, and stearate from (+)-2 : 3-dibromopropan-1-ol proves that the esters had not become equilibrated with the symmetrical isomers, but it is not known to what thermal treatment the products had been subjected.[10] Of more significance, therefore, is that fact that 2 : 3-dibromopropyl lævulate apparently remained substantially a single compound after distillation at 208—210°/40 mm., since it gave only one semicarbazone and one phenylhydrazone.[11] Finally, the butyrates prepared from 2 : 3-dibromopropan-1-ol and 1 : 3-dibromopropan-2-ol were shown [3] to be distinct despite having been distilled at 118°/6·5 mm. It thus seems reasonable to suppose that the aliphatic esters of the dibromopropanols undergo thermal rearrangement less readily than the benzoates (isomerised at 120°/0·4 mm.). The apparent slow conversion of 2 : 3-dibromopropyl acetate into its isomer on prolonged heating in the presence of hydrogen chloride is probably, as Edwards and Hodges suggested,[3] an example of acid-catalysed rather then truly thermal rearrangement.

The observed order of ease of thermal rearrangement in the substituted benzoates (*p*-anisates > *p*-chlorobenzoates ⩾ 3 : 5-dinitrobenzoates) is the reverse of that to be expected if the acyloxy-group migrated as an anion, but would be consistent with a mechanism involving cyclisation to a resonating dioxolanium structure.[12] It is therefore suggested that thermal interconversion of isomeric dibromo-esters (I and III) in non-polar solvents containing no added acid may proceed by intramolecular rearrangement through the hypothetical ion-pair (II). Such an intermediate might be supposed to be formed more readily when the substituent (R) represents a suitable aromatic radical rather than when it is alkyl, since it might then be stabilised by contributions from additional resonance forms (*e.g.*, IV). It is, however, realised that, as in other cases of anionotropic rearrangement,[13] different mechanisms (including the acid-catalysed process advocated by Edwards and Hodges [3]) may be more appropriate under other conditions.

At the outset of the present investigation it was expected that addition of bromine to allyl esters would provide a useful alternative route to 2 : 3-dibromo-esters but, as mentioned in a preliminary note,[14] the reaction was found in several cases to be complex. The crude oil from the addition of bromine to allyl *p*-anisate in dry chloroform at room temperature was separated by treatment with methanol into 45% of the expected 2 : 3-dibromopropyl *p*-anisate and 32% of the isomeric ester from 1 : 3-dibromopropan-2-ol. A non-vicinal

[9] Doyle, Hunter, and Nayler, unpublished work.
[10] Abderhalden and Eichwald, *Ber.*, 1914, **47**, 2880.
[11] Sah and Ma, *J. Amer. Chem. Soc.*, 1932, **54**, 3271.
[12] Winstein and Buckles, *J. Amer. Chem. Soc.*, 1942, **64**, 2780.
[13] Braude, Turner, and Waight, *Nature*, 1954, **173**, 863.
[14] Nayler, *Chem. and Ind.*, 1958, 863.

dibromide was similarly isolated in 14% yield from allyl *p*-chlorobenzoate, although the 2 : 3-dibromopropyl ester was the main product. These four crystalline dibromides were identified by comparison with authentic esters prepared from 2 : 3-dibromopropan-1-ol and 1 : 3-dibromopropan-2-ol. The oily nature of the crude dibromides obtained from allyl benzoate and *p*-toluate suggested that they too were probably mixtures, but allyl 2 : 4-dichlorobenzoate gave only the 2 : 3-dibromopropyl ester.



Dibromides have been prepared before from a number of allyl esters, but in no case has the isolation of more than one product been reported. The crystalline products from allyl palmitate,[15] *p*-nitrobenzoate,[16] and 3 : 5-dinitrobenzoate [16] must have been the normal 2 : 3-dibromopropyl esters because their melting points were different from those of the esters of 1 : 3-dibromopropan-2-ol, of which the palmitate and *p*-nitrobenzoate had been prepared previously [15,16] and the 3 : 5-dinitrobenzoate was obtained in the present work. Liquid dibromides have been less well characterised, but the product from allyl lævulate was evidently essentially a single compound, identical with that obtained from 2 : 3-dibromopropanol and lævuloyl chloride, since both specimens gave only one semicarbazone and one phenylhydrazone.[11]

Apparently allyl esters of aliphatic acids and the stronger aromatic acids (*e.g.*, *p*-nitro-, 3 : 5-dinitro-, and 2 : 4-dichloro-benzoic acid) give exclusively normal dibromides, whilst the tendency to form a mixture of vicinal and non-vicinal dibromides is characteristic of the weaker aromatic acid derivatives. The dibromides of the latter group are those which undergo ready thermal isomerisation, but the formation of a proportion of abnormal bromine adduct in such cases cannot be ascribed to this cause since the conditions are far too mild. Nevertheless, the correspondence suggests a similarity in reaction mechanism.

In suitable circumstances cyclisation might be supposed to compete with the second stage of the normal addition of bromine to an allyl ester (V ⟶ VI ⟶ I). A fairly high electron-density at the acyl-oxygen atom of the intermediate (VI) could be expected to favour formation of the hypothetical structure (II), as would a substituent (R) which could confer additional resonance stability on the cyclic structure. As in the thermal isomerisations, these requirements appear to be met when R represents an aryl radical containing neither a strongly electron-attracting group nor an *ortho*-substituent which would place steric restrictions on resonance. Participation of the ion-pair (II) in the addition of bromine to an allyl ester would result in the formation of a proportion of the non-vicinal dibromide (III).

The possible significance of cyclic intermediates in the addition of bromine to certain allyl derivatives has been discussed by Winstein and his collaborators. They concluded [17] that the structure (II; R = Me) did not participate in the addition of bromine to allyl acetate, because no ortho-ester (VII; R = Me) could be detected when the reaction was run in methanol. The oxazolinium bromides (VIII; R = Ph or C_6H_4·OMe-*p*), which may

[15] Fairbourne and Cowdrey, *J.*, 1929, 129.
[16] Fairbourne and Foster, *J.*, 1926, 3146, 3148.
[17] Winstein and Goodman, *J. Amer. Chem. Soc.*, 1954, **76**, 4368.

be regarded as stable nitrogen analogues of the hypothetical intermediate (II), were, however, obtained, together with *N*-(2 : 3-dibromopropyl)-amides, in the addition of bromine to 3-benzamidopropene and its *p*-methoxy-derivative.[18]

Experimental

Infrared absorption spectra were kindly determined by Mr. H. D. C. Rapson and Mr. K. Austin using a Grubb-Parsons double-beam spectrometer. The specimens were examined as liquid films (the pure benzoates being first melted by gentle warming) between sodium chloride plates.

2 : 3-*Dibromopropyl Benzoate*.—Benzoyl chloride (14·1 g.) and 2 : 3-dibromopropan-1-ol (21·8 g.) were heated together on the steam-bath under reflux until evolution of hydrogen chloride ceased (3 hr.). The colourless oil was cooled, diluted with ether, washed with sodium hydrogen carbonate solution and then with water, and dried. After removal of the solvent under reduced pressure, the residual oil was rubbed with methanol at low temperature, whereupon it crystallised. The white solid was collected and washed with very cold methanol (yield 26·1 g., 81%; m. p. 31—32°). 2 : 3-*Dibromopropyl benzoate* was purified by dissolution in methanol (45 ml.) at room temperature, followed by strong cooling to give small colourless rods, m. p. 33—34° (Found: C, 37·8; H, 3·4. $C_{10}H_{10}O_2Br_2$ requires C, 37·3; H, 3·1%), $\nu_{max.}$ 7·05, 7·27, 7·6, 7·8, 8·0, 8·5, 8·7, 9·35, 9·75, 10·28, 10·7 μ.

2-*Bromo*-1-*bromomethylethyl Benzoate*.—Benzoyl chloride (7·0 g.) and 1 : 3-dibromopropan-2-ol (10·9 g.) were heated on the steam-bath for 9 hr. and the product was isolated as described for the isomer. Crude 2-*bromo*-1-*bromomethylethyl benzoate* (12·5 g., 75%), m. p. 29—30°, was purified by dissolution in methanol (25 ml.) at room temperature, followed by strong cooling to give hexagonal plates, m. p. 32—33° (Found: C, 37·6; H, 3·2. $C_{10}H_{10}O_2Br_2$ requires C, 37·3; H, 3·1%), $\nu_{max.}$ 7·04, 7·43, 7·53, 7·62, 7·85, 8·05, 8·35, 9·35, 9·75, 10·07, 10·45, 10·7, 11·9 μ. Admixture with 2 : 3-dibromopropyl benzoate at room temperature resulted in liquefaction.

Preparation of Dibromopropyl Esters in Presence of Pyridine.—The appropriate acid chloride (0·1 mole) in dry chloroform (30 ml.) was added during 15 min. to a stirred ice-cold mixture of pyridine (20 ml.), chloroform (30 ml.), and the dibromopropanol (21·8 g., 0·1 mole). The mixture was stirred at 0° for 1 hr., set aside overnight at room temperature, poured into ice-water, and acidified with hydrochloric acid. The layers were separated and the aqueous phase was twice extracted with chloroform. The combined chloroform solutions were washed with sodium hydrogen carbonate solution, then with water, dried, and evaporated under reduced pressure. Products, if oily, were triturated with methanol at low temperature. Details are in Table 1. 2-Bromo-1-bromomethylethyl 3 : 5-dinitrobenzoate was recrystallised from chloroform; in other cases methanol was used. Compounds melting below 40° were purified by dissolution in methanol at room temperature, followed by strong cooling. When the isomeric esters had similar m. p.s marked depression was observed on admixture. References in this paper to " authentic specimens " are to compounds prepared in this way.

Thermal Rearrangement of p-*Anisates and* p-*Chlorobenzoates*.—A solution of the ester (5 g.) in the dry solvent (30 ml.) (Table 2) was refluxed for the period stated, then evaporated under reduced pressure. The gummy residue was rubbed with methanol and set aside at room temperature for a few hours, and the white solid collected: it usually consisted of fairly pure 2-bromo-1-bromomethylethyl ester. The filtrate was cooled strongly to give a second crop which frequently contained both isomers, which were separated by further treatment with methanol. Concentration of the mother-liquor gave a third crop, usually consisting of fairly pure 2 : 3-dibromopropyl ester. Further purification of the various crops was effected in the usual way. The recoveries noted in Table 2 refer to materials which melt no more than a few degrees lower then the pure compounds and show no depression of m. p. on admixture with the latter.

Allyl Esters.—Allyl alcohol (8 g.) and *p*-toluoyl chloride (14·3 g.) were heated under reflux on the steam-bath for 4 hr., then distilled to give *allyl* p-*toluate* (59%), b. p. 117—120°/11 mm. A redistilled specimen had b. p. 117°/11 mm., n_D^{20} 1·5135 (Found: C, 75·4; H, 7·1. $C_{11}H_{12}O_2$ requires C, 75·0; H, 6·9%).

Similar procedures gave *allyl* p-*anisate* (89%), b. p. 78—80°/0·03 mm., n_D^{20} 1·5354 (Found:

[18] Goodman and Winstein, *J. Amer. Chem. Soc.*, 1957, **79**, 4788.

C, 68·8; H, 6·6. $C_{11}H_{12}O_3$ requires C, 68·7; H, 6·3%), p-*chlorobenzoate* (74%), b. p. 129—130°/14 mm., n_D^{20} 1·5360 (Found: C, 61·2; H, 4·7; Cl, 18·3. $C_{10}H_9O_2Cl$ requires C, 61·1; H, 4·6; Cl, 18·0%), and 2 : 4-*dichlorobenzoate* (86%), b. p. 143—144°/14 mm., n_D^{19} 1·5533 (Found: C, 51·5; H, 3·4; Cl, 31·0. $C_{10}H_8O_2Cl_2$ requires C, 52·0; H, 3·5; Cl, 30·7%).

Addition of Bromine to Allyl Esters.—(a) *To allyl* p-*anisate.* Bromine (14·5 g.) in dry chloroform (20 ml.) was added dropwise to a stirred solution of allyl *p*-anisate (17·4 g.) in chloroform (35 ml.). When decolorisation was complete (30 min.) the solution was washed with sodium hydrogen carbonate solution, then with water, dried, and evaporated under reduced pressure.

TABLE 1.

Ester	Yield (%)	Form	M. p.	Formula	Found (%) C	Found (%) H	Required (%) C	Required (%) H
2 : 3-Dibromopropyl esters.								
Benzoate	76	Rods	33—34°	$C_{10}H_{10}O_2Br_2$	37·8	3·4	37·3	3·1
p-*Toluate*	81	Needles	29—30	$C_{11}H_{12}O_2Br_2$	39·4	3·4	39·3	3·6
p-*Anisate*	78	Plates	38—39	$C_{11}H_{12}O_3Br_2$	37·5	3·5	37·5	3·4
o-*Chlorobenzoate*	79	Plates	32—33	$C_{10}H_9O_2Br_2Cl$	33·4	2·5	33·7	2·6
p-*Chlorobenzoate*	71	Prisms	30—31	$C_{10}H_9O_2Br_2Cl$	33·9	2·9	33·7	2·6
2 : 4-*Dichlorobenzoate*	67	Rhombs	39—40	$C_{10}H_8O_2Br_2Cl_2$	30·7	2·4	30·7	2·1
p-Cyanobenzoate	64	Prisms	78—79 *	$C_{11}H_9O_2NBr_2$	38·3	2·9	38·1	2·6
p-Nitrobenzoate †	57	Plates	53—54	$C_{10}H_9O_4NBr_2$	32·8	2·4	32·7	2·5
3 : 5-Dinitrobenzoate †	70	Plates	84—85	$C_{10}H_8O_6N_2Br_2$	29·5	2·3	29·2	2·0
2-Bromo-1-bromomethylethyl esters.								
Benzoate	62	Plates	32—33	$C_{10}H_{10}O_2Br_2$	37·6	3·2	37·3	3·1
p-*Toluate*	59	Plates	41—42	$C_{11}H_{12}O_2Br_2$	39·6	3·9	39·3	3·6
p-*Anisate*	66	Plates	95—96	$C_{11}H_{12}O_3Br_2$	37·8	3·5	37·5	3·4
o-*Chlorobenzoate*	60	Rods	39—40	$C_{10}H_9O_2Br_2Cl$	33·9	2·9	33·7	2·6
p-*Chlorobenzoate*	83	Needles	107—108	$C_{10}H_9O_2Br_2Cl$	33·4	2·7	33·7	2·6
2 : 4-*Dichlorobenzoate*	68	Needles	73—75	$C_{10}H_8O_2Br_2Cl_2$	30·3	2·4	30·7	2·1
p-*Cyanobenzoate*	53	Needles	80—81	$C_{11}H_9O_2NBr_2$	38·3	3·0	38·1	2·6
p-Nitrobenzoate ‡	54	Needles	78—79	$C_{10}H_9O_4NBr_2$	32·6	2·6	32·7	2·5
3 : 5-*Dinitrobenzoate*	67	Plates	139	$C_{10}H_8O_6N_2Br_2$	29·2	2·2	29·2	2·0

* Not depressed by admixture with the product obtained by Chow and Gisvold's method.[7] † Previously prepared from the allyl esters and bromine.[16] ‡ Previously prepared from 1 : 3-dibromopropan-2-ol and *p*-nitrobenzoyl chloride in quinoline.[16]

TABLE 2. *Thermal rearrangements (reflux for 24 hr.).*

Ester	Solvent	Products (%) (I)	Products (%) (III)	Ester	Solvent	Products (%) (I)	Products (%) (III)
	p-*Anisates*				p-*Chlorobenzoates*		
I	Toluene	84	7	I	Toluene	92	0
III	,,	12	77	III	,,	0	91
I	Xylene	47	39	I	Xylene	66	24
I	,, *	42	38	III	,,	32	56
III	,,	45	41	I	,, †	47	42
III	,, *	44	40	III	,, †	44	41
				I	AcOH	20	26
				III	AcOH	13	34

* Stirred with $CaCO_3$ (5 g.). † 72 hr.

The residual oil was rubbed with several portions of methanol to leave 2-bromo-1-bromomethylethyl *p*-anisate (10·1 g., 32%), m. p. 90—93° raised to 94—96° by crystallisation from hot methanol and not depressed by admixture with an authentic specimen. From the mother-liquors there was recovered 2 : 3-dibromopropyl *p*-anisate (14·4 g., 45%), m. p. 32—33° raised to 38—39° by crystallisation from methanol below room temperature and not depressed by admixture with an authentic specimen.

(b) *To allyl* p-*chlorobenzoate.* When bromine (17·5 g.) in chloroform (20 ml.) was added dropwise to allyl *p*-chlorobenzoate (21·5 g.) in chloroform (40 ml.) decolorisation was complete in 80 min. Working up as in (a) gave an oil which, when rubbed with methanol (100 ml.), slowly gave a white solid (4·67 g.), m. p. 99—103°. Concentrating and cooling the filtrate gave several further crops of low-melting solid (29·5 g. in all). The latter were combined and treated with methanol (160 ml.) whereupon the greater part dissolved, but a small residue was further

crystallised from hot methanol to give 0·78 g. of material, m. p. 105—107°. The more soluble principal component, recovered from the mother-liquor, had m. p. 29—31° and crystallised from methanol below room temperature in prisms, m. p. 30—31°, not depressed by admixture with authentic 2 : 3-dibromopropyl *p*-chlorobenzoate. The combined crops (5·45 g., 14%) of the less soluble and higher-melting product were further crystallised from hot methanol to give the pure isomer, m. p. and mixed m. p. 107—108°.

(c) *To allyl* 2 : 4-*dichlorobenzoate.* Bromine (8·8 g.) in chloroform (20 ml.), added dropwise to allyl 2 : 4-dichlorobenzoate (12·6 g.) in chloroform (70 ml.), was decolorised in 6 hr. The crude oil, obtained as in (a), on treatment with cold methanol gave 2 : 3-dibromopropyl 2 : 4-dichlorobenzoate (13·5 g.), m. p. 38—39°. Recrystallised from methanol it had m. p. and mixed m. p. 39—40°.

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36. *Hydrothermal Chemistry of the Silicates. Part VIII.* Low-temperature Crystal Growth of Aluminosilicates, and of Some Gallium and Germanium Analogues.*

By R. M. BARRER, J. W. BAYNHAM, F. W. BULTITUDE, and W. M. MEIER.

The hydrothermal method has been used to study the crystallisation of aluminosilicates from 60° to 250°. Hydrous gels of compositions $Na_2O,Al_2O_3,nSiO_2$ ($1 \leqslant n \leqslant 12$) in presence of excess of sodium hydroxide yielded analcite, mordenite, zeolites of the harmotome, faujasite and chabazite groups, Linde Molecular Sieve A, a zeolitic phase related to rhodesite, basic sodalite, basic nosean, and a phase related to nepheline hydrate. The species formed have been characterised by optical, *X*-ray, and chemical methods.

The corresponding crystallisation of mixed Na,K-aluminosilicate gels has been compared with that of the homoionic Na- and K-gels. From the mixed gels in the interval 60° to 250° phases in the analcite–leucite, the chabazite, harmotome–phillipsite, felspar, and kalsilite groups were prepared. In addition, boehmite, quartz, and a synthetic zeolite were obtained.

When Ga replaced Al and Ge replaced Si in Na-gels, crystallisation of alkaline gels at 100° yielded, as gallosilicate, a fibrous zeolite resembling thomsonite; as aluminogermanates, zeolites of faujasite type, and an analogue of Linde Sieve A and of harmotome; and as gallogermanates, zeolites again resembling thomsonite, faujasite, and Linde Sieve A. If Ga or Ge replace Al or Si, the unit cells of the crystalline phases become slightly larger.

Attention has been given to the mechanism of growth of diverse structural patterns from alkaline hydrothermal magmas.

THE lower-temperature crystallisation fields of aluminosilicates of lithium,[1] sodium,[2] potassium,[3] rubidium,[4] thallium,[5] and cæsium [4] were previously studied hydrothermally;

* Part VII, *J.*, 1956, 2882.

[1] Barrer and White, *J.*, 1951, 1167.
[2] *Idem*, *J.*, 1952, 1561.
[3] Barrer and Baynham, *J.*, 1956, 2882.
[4] Barrer and McCallum, *J.*, 1953, 4029.
[5] Taylor, *J.*, 1949, 1253.

XUM

the chemistry and properties of some of the species obtained, among which were many zeolites, were investigated,[6-9] and certain aspects surveyed.[10]

Zeolites appear to be formed naturally at as low as 60° at Wairakei, New Zealand,[11] and in the temperature range 60—150° several potassium zeolites have been synthesised,[3,8] for example, a series of chabazite phases and phases related to the harmotome–phillipsite group. Since the hydrothermal crystallisation of sodium aluminosilicates had been investigated at or above 150°, and had resulted in the synthesis of two zeolites only (analcite [2,12-15] and mordenite [2,16]), we have now studied the crystallisation field of sodium aluminosilicates down to lower temperatures. Zeolites are " filled " structures, the filler being water, and should be more readily formed the lower the temperature, owing to the volatility of the filler. The synthesis of additional synthetic zeolites, some of which are Na-rich, has already been indicated.[1-9]

Barrer, Hinds, and White [6] showed that mineral metamorphoses in hydrothermal media could take a course in mixed aqueous electrolytes, *e.g.*, sodium and potassium carbonates, different from that in either single electrolyte. Accordingly we have also studied the crystallisation of $(Na,K)_2O,Al_2O_3,nSiO_2,mH_2O$ gels containing two cations, in relation to crystallisation of these gels containing only one cation, Na or K. Finally, experiments have been made to see how readily one can replace Al by Ga and Si by Ge and still obtain the same structural types. Goldsmith [17,18] showed that such replacements are possible in leucite and in felspars, and that a gallium-containing thomsonite can be synthesised hydrothermally from a gallium-containing glass. Similarly Eitel [19] demonstrated, by pyrolytic synthesis of phlogopite-micas, that analogous replacements of Si by Ge can occur in this layer-lattice mineral.

Experimental

(a) *Preparation of* Na-*gels, and Crystallisation Conditions.*—Silica was in the form of a stable dispersion " Syton 2-X " (Monsanto Chemicals Ltd.) and contained 30% (w/w) of SiO_2, had pH ~10, specific gravity 1·2, and average particle diameter 250 Å. There was a trace of chloride.

Alumina was initially introduced as aluminium hydroxide prepared by the action of cold water on lightly amalgamated aluminium foil.[20] Better crystallisations were achieved by using " Alfloc " sodium aluminate (Imperial Chemical Industries Limited) which contained ~87% (w/w) of $NaAlO_2$, a trace of iron, and the remainder free sodium hydroxide. Subsequent results refer to crystallisations achieved from gels containing " Alfloc."

Gels of compositions $Na_2O,Al_2O_3,nSiO_2$ ($1 \leqslant n \leqslant 12$) were prepared by dissolving " Alfloc " in water, filtering off the precipitated ferric hydroxide, and adding suitable quantities of " Syton." The SiO_2 gelatinised in presence of sodium cations and so continual stirring during the addition of the " Syton " and for about ½ hr. afterwards was necessary to disperse the silica evenly. " AnalaR " sodium hydroxide was added so that either 100%, 200%, or 300% molar excess of sodium hydroxide over that required for the ratio of base : alumina to be 1 : 1 was present.

Between 60° and 110° crystallisations were carried out in Pyrex glass tubes of ~1·25 cm.

[6] Barrer, Hinds, and White, *J.*, 1953, 1466.
[7] Barrer, Baynham, and McCallum, *J.*, 1953, 4035.
[8] Barrer and Baynham, *J.*, 1956, 2892.
[9] Gard, Barrer, and Baynham, *J.*, 1955, 2480.
[10] Barrer, *Trans. Brit. Ceram. Soc.*, 1957, **56**, 155.
[11] Steiner, *Econ. Geol.*, 1953, **48**, 1.
[12] Friedman, *J. Geol.*, 1951, **59**, 14.
[13] von Nieuwenberg and Blumendahl, *Rec. Trav. chim.*, 1931, **50**, 989.
[14] Straub, *Ind. Eng. Chem.*, 1936, **28**, 113.
[15] Guyer, Ineichen, and Guyer, *Helv. Chim. Acta*, 1957, **40**, 1603.
[16] Barrer, *J.*, 1948, 2158.
[17] Goldsmith, *J. Geol.*, 1950, **58**, 518.
[18] *Idem*, *Mineralog. Mag.*, 1952, **29**, 952.
[19] Eitel, Proc. Int. Symp. on Reactivity of Solids, Gothenburg, 1954, Part I, 335.
[20] Weiser and Milligan, *J. Phys. Chem.*, 1937, **41**, 1029; *Chem. Rev.*, 1939, **25**, 1.

XUM

internal diam. Charges of ½ g. of gel, calculated as dry weight of the constituents, in 10 ml. of total mixture were sealed in the tubes so that the latter had an internal capacity of ~20 ml. At higher temperatures the glass was appreciably attacked by the gel, so stainless steel autoclaves of ~20 ml. capacity were employed.[21] The gels were heated in electrically heated ovens, thermostatically controlled to ±1°, and after any desired length of treatment the glass tubes were cooled in air, the steel autoclaves quenched in cold water, and the product filtered off, washed with hot water until free from alkali, and air-dried. Large-scale preparations were made in an electrically heated autoclave of 1 l. capacity (Chas. W. Cook and Sons Ltd.).

(b) *Preparation of Mixed* Na, K-*gels, and Crystallisation Conditions.*—Alumina, prepared as above from lightly amalgamated aluminium foil, was mixed with the appropriate amount of " AnalaR " potassium hydroxide solution. The product was then mixed with " Syton 2-X " with continuous stirring. Various aqueous gels were thus prepared, usually of oxide composition $K_2O,Al_2O_3,nSiO_2,mH_2O$ ($2 \leqslant n \leqslant 12$). To these gels various amounts of sodium hydroxide solution were then added, and the gel finally crystallised at various temperatures (see Tables 3 and 4) and for between 1 and 18 days as required.

(c) *Preparation of* Na-*gels containing* Ga *and* Ge, *and Crystallisation Conditions.*—Sodium gallosilicate, gallogermanate and aluminogermanate gels were prepared, by use of sodium aluminate (" Alfloc "), sodium gallate, silica sol (" Syton 2X "), and sodium germanate as appropriate components. The gallate and germanate were prepared as follows.

3·75 g. of Ga_2O_3 (40 mequiv.) were dissolved in 25 ml. of aqueous sodium hydroxide (30%) and 50 ml. of water on the water-bath. The filtered solution was diluted to 400 ml. and acidified with hydrochloric acid (to pH ~1), and the hot solution finally neutralised with ammonia. The precipitated $Ga(OH)_3$ was filtered off, washed with hot water, and dissolved in 30 ml. of 2N-sodium hydroxide. Water was then added to make up 80 ml. An apparently colloidal, opaque alkaline dispersion was obtained, which may be regarded as a 0·5M-$NaGaO_2$ dispersion. [More than 3 NaOH per $Ga(OH)_3$ were necessary to obtain clear solutions.]

4·20 g. (40 mmoles) of GeO_2 were next dissolved in 20 ml. of aqueous sodium hydroxide (30%) on the water-bath, and the solution filtered after dilution with 50 ml. of water. The filtrate was acidified with concentrated hydrochloric acid, after which germanic acid gel was precipitated by adding aqueous ammonia (to pH ~6—7), and was washed thoroughly with hot water. The wet gel was then dissolved in 40 ml. of 2N-sodium hydroxide, and water added to make 80 ml. of 0·5M-sodium germanate solution.

" Syton 2X " was diluted to give a 1M-colloidal solution, and " Alfloc " was dissolved in a small amount of water and filtered to remove insoluble matter such as ferric hydroxide. It was then diluted to 1M, and a sample analysed. The excess of alkali corresponded to 0·25 mmole of sodium hydroxide per ml.

Measured amounts of the appropriate pairs of solutions or suspensions were then mixed with stirring to give reactant mixtures containing 0·5 g. of solid per 10 ml. No extra alkali was added since it was already in excess. The mixtures were then rotated in sealed glass tubes at 100° in thermostatic air-ovens. The crystallisations were allowed between 7 and 46 hr., after which the solid products were filtered off and washed thoroughly with hot water.

(d) *Examination of Products.*—A Leitz IIIC polarising microscope and a Vickers projection microscope were used to examine the products optically, but where the crystals were too small so to characterise their habit, electron micrographs were taken on a Metrovic EM3 by Dr. J. A. Gard of Aberdeen University. Refractive indices were determined to ±0·005 unit in white light.

X-Ray powder photographs were taken on 9 cm. Debye–Scherrer cameras and a " Nonius " Guinier camera, the Cu-K_α radiation used being generated by a Hilger HRX unit. Where possible, unit-cell dimensions were determined.

Products obtained in 100% yield were analysed by standard methods, the procedures followed being those recommended by Groves.[22]

Results.—Crystalline sodium aluminosilicates. The minerals observed are listed in Table 1, the reference letter being either that used in the previous higher-temperature investigation [2] or in a continuation of it.

The results of the crystallisations, the yields being determined by optical examination, are given in Table 2. The fields of growth of the major species are clarified in Fig. 1 (which includes

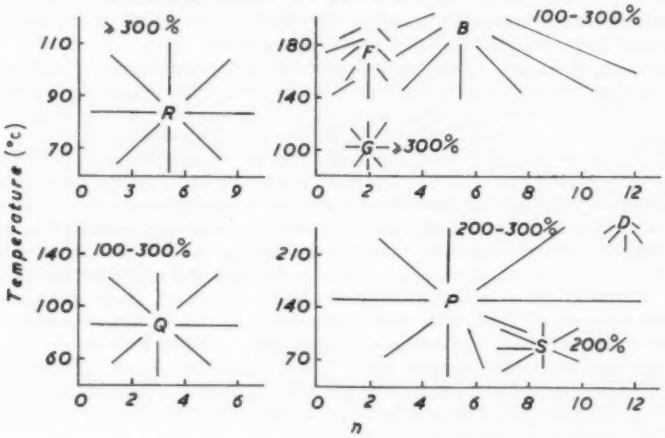
[21] Barrer, *J.*, 1948, 127.
[22] Groves, " Silicate Analysis," Allen and Unwin, London, 1951.

experiments, particularly for Na-*R*, not recorded in Table 2), but it must be emphasised that only approximate areas of crystallisation can be delineated since no attempt was made to define the exact phase boundary of each species. Yields often diminish rather slowly along either the composition or the temperature axis.

Crystallisation was often very rapidly and easily accomplished. Thus 2 or 3 hr. were sufficient to obtain good yields of species *Q* at 85—110° from alumina-rich gels. Slightly longer was required as the silica content of the gel increased. Crystallisation was also better and more rapid from gels containing a large excess of sodium hydroxide (300%), the effect being especially marked at 60° and 85°.

The preparation and characteristics of individual species will now be considered.

FIG. 1. *Fields of growth of minerals synthesised from* $Na_2O,Al_2O_3,nSiO_2,mH_2O$ *gels with excess of sodium hydroxide added (percentages shown).*



Zeolites. Species *P*, related to the natural harmotome–phillipsite groups of zeolites, occurred as very small (~2 μ) irregular crystals (Plate 1) from gels $n = 1$ to $n = 12$ over the range 60—250°. The crystals exhibited no birefringence, but the refractive indices decreased from 1·493 for a sample grown from a gel of $n = 2$, through 1·475 for a gel of $n = 5$, to 1·455 for $n = 8$. Optimum yields were obtained after one day's treatment at 110° with 200% or 300% excess of alkali present, since under these conditions recrystallisation of species *Q*, which was usually the primary nucleation product, to this mineral was rapid.

TABLE 1. *Summary of crystalline species.*

Ref. letter	Name or natural counterpart	Oxide formula	Mineral class
B	Analcite	$Na_2O,Al_2O_3,4SiO_2,2H_2O$	Zeolite
D	Mordenite	$Na_2O,Al_2O_3,10SiO_2,6{\cdot}7H_2O$	Zeolite
F	" Basic " nosean	$Na_2O,Al_2O_3,2SiO_2,xNaOH,yH_2O$	Felspathoid
I	" Basic " sodalite	$Na_2O,Al_2O_3,2{\cdot}1SiO_2,2NaOH,1{\cdot}5H_2O$	Felspathoid
P	Phases of harmotome–phillipsite group	$Na_2O,Al_2O_3,3{\cdot}3SiO_2,4{\cdot}3H_2O$ to $Na_2O,Al_2O_3,5{\cdot}3SiO_2,5{\cdot}7H_2O$	Zeolites
Q	Species *Q*	$Na_2O,Al_2O_3,2SiO_2,4H_2O$	Zeolite
R	Phases of faujasite group	$Na_2O,Al_2O_3,2{\cdot}4SiO_2,6{\cdot}7H_2O$ to $Na_2O,Al_2O_3,3{\cdot}3SiO_2,7H_2O$	Zeolites
S	Phases of chabazite-gmelinite group	$Na_2O,Al_2O_3,5SiO_2,5{\cdot}4H_2O$	Zeolites
T	Nepheline hydrate III	$Na_2O,Al_2O_3,2SiO_2,xH_2O$?	Felspathoid
U	Species U	—	Zeolite (?)

The composition of the crystals varied from $Na_2O,Al_2O_3,3{\cdot}3SiO_2,4{\cdot}3H_2O$ to $Na_2O,Al_2O_3,5{\cdot}3SiO_2,5{\cdot}7H_2O$. Variations in the unit cell were also noted, some samples being cubic, $a = 10{\cdot}0$ Å, and others tetragonal, $a = 10{\cdot}0$ Å, $c = 9{\cdot}8$ Å, the *c* parameter also varying slightly between samples. *d*-Spacings are given in Table 3.

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PLATE 1. *Species P* × 4400.

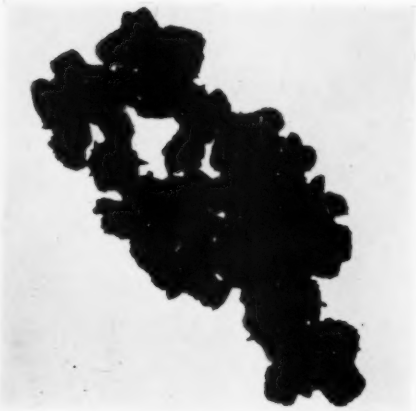

PLATE 2. *Rhombohedral species P* × 628.

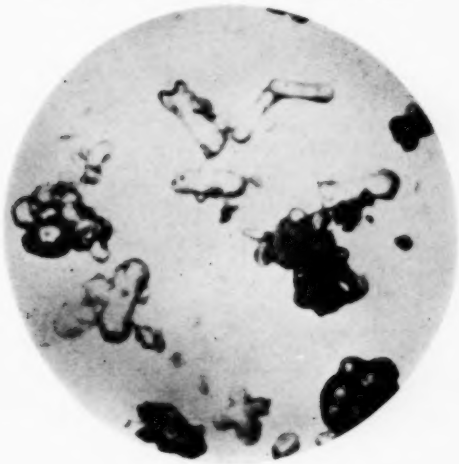

PLATE 3. *Species Q* × 3000.

PLATE 4. *Species R* × 13,000.

[*To face p.* 198.

XUM

PLATE 5. *Species S* × 628.

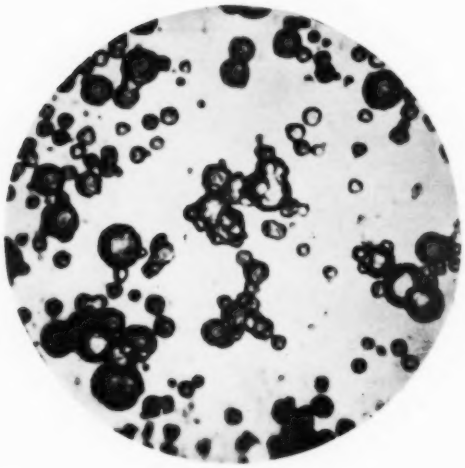

PLATE 6. *Species U* × 4000.

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Two preparations, having orthorhombic unit cells, $a = 14{\cdot}1$, $b = 14{\cdot}0$, $c = 9{\cdot}8$, were grown at 250° from gels $n = 5$ with about 200% excess of alkali but syntheses were not reproducible. These orthorhombic forms grew in a variety of crystal habits, the most common being rods slightly thickened at each end which occasionally exhibited cross twinning (Plate 2). This resembles the mode of growth of species K-*M* [3], which also had a very similar *X*-ray powder pattern (Table 3). The inter-relations of the unit cells of these phases will be discussed in another paper.[24]

Species *Q* is a purely synthetic zeolite with no natural counterpart but its *X*-ray pattern identifies it with the synthetic zeolite type *A* described by Breck *et al.*[25, 26] It grew as very

TABLE 2. *Products of crystallisation of sodium aluminosilicate gels.*

In all cases pH of mother-liquor >10·5.
No brackets = 100% molar excess of NaOH, *i.e.*, gel was $2Na_2O,Al_2O_3,nSiO_2$.
( ) = 200% molar excess of NaOH, *i.e.*, gel was $3Na_2O,Al_2O_3,nSiO_2$.
[ ] = 300% molar excess of NaOH, *i.e.*, gel was $4Na_2O,Al_2O_3,nSiO_2$.
Q ⟶ *P* signifies that species *Q* recrystallised to species *P* very readily.

Temp.	$n = 1$	$n = 2$	$n = 3$	$n = 4$
60°	Moderate *Q* (Moderate *Q*) [Moderate *Q*]	Poor *Q* (Moderate *Q*) [Moderate *Q*]	Poor *Q* (Moderate *Q*) [Moderate *Q*]	No crystallisation (Moderate *Q*) [Moderate *Q*]
85°	Good *Q* (Good *Q*) [Good *Q*]	Good *Q* (Good *Q*) [Good *Q*]	Poor *Q* (Good *Q*) [Good *Q*]	No crystallisation after 1 day (Poor *Q*) [Moderate *Q*]
110°	Good *F* + some *Q* (Good *F* + some *Q*) [V. good *P* + some *Q*]	Good *Q* ⟶ *P* (Good *Q* ⟶ *P*) [V. good *P*]	Good *Q* ⟶ *P* (Good *Q* ⟶ *P*) [V. good *P*]	Good *Q* ⟶ *P* (V. good *P*) [V. good *P*]
150°	Good *F* (Good *F*) [Good *F*]	Good *F* + some *B* (Good *B* + *F*) [Good *F*]	Good *F* + *B* (Good *F* + *B*) [Good *F* + some *P*]	Good *B* + some *P* (Good *B*) [Good *B*]
200°	Good *F* (Good *F*) [Good *F*]	Good *F* (Good *B* + *F*) [Good *B* + some *F* and *T*]	Good *F* + some *B* and *P* (Good *F* + some *P*) [Good *B*]	Good *B* + some *F* (V. good *B*) [V. good *B*]
250°	Good *F* (Good *F* + some *B* and *P*) [Good *F* + some *P*]	Good *B* + *F* (Good *B* + *F*) [Good *B* + *F*]	Good *F* + some *P* and *B* (Good *B* and *F* + some *P*) [Good *P* + *F*]	Good *B* + *F* + *P* (Good *B* + some *F* and *P*) [V. good *B*]
	$n = 5$	$n = 6$	$n = 7$	$n = 8$
60°	No crystallisation (Moderate *Q*) [Good *Q* + *R*]	V. poor *Q* (Poor *Q*) [Poor *P* + some *R*]	No crystallisation (No crystallisation) [Poor *S* + some *R*]	No crystallisation observed even with 300% excess of NaOH
85°	Poor *Q* (Poor *Q*) [Poor *Q*]	Moderate *Q* (Moderate *Q*) [Good *P*]	No crystallisation (No crystallisation) [Moderate *P*]	No crystallisation (No crystallisation) [Good *S*]
110°	Good *Q* (Good *P*) [Good *P*]	Moderate *Q* (Good *P*) [Good *P*]	No crystallisation (Good *P*) [Good *P* + *S*]	Good *S* + some *P* (Good *P* + *S*) [Good *P* + *S*]
150°	Good *B* + some *P* (Good *B*) [Good *B*]	Good *P* (Good *B*) [Good *B* + some *P*]	Good *B* + *P* (Good *P*) [Good *B* + *P*]	Good *B* (Good *B*) [Good *B* + *P*]
200°	Good *B* + *P* (Good *B* + trace *P*) [Good *B* + *P*]	Good *B* (Good *B*) [Good *B*]	Good *B* + *P* (Good *B*) [Good *B* + *P*]	Good *B* (Good *B*) [Good *B* + *P*]
250°	Good *B* (Good *B*) [Good *B*]	Good *B* + *P* (Good *B* + *P*) [Good *B* + *P*]	Good *B* + *P* (Good *B*) [Good *B* + *P*]	[Good *B* + *P*] (Good *B*) [Good *B* + *P*]

[23] Strunz, *Neues Jb. Min.*, 1956, **11**, 250.
[24] Barrer, Bultitude, and Kerr, unpublished work.
[25] Breck, Eversole, Milton, Reed, and Thomas, *J. Amer. Chem. Soc.*, 1956, **78**, 5963.
[26] Reed and Breck, *ibid.*, p. 5972.

XUM

TABLE 2. (*Continued.*)

Temp.	$n = 9$	$n = 10$	$n = 11$	$n = 12$
60°	No crystallisation even with 300% excess of NaOH	No crystallisation even with 300% excess of NaOH	No crystallisation even with 300% excess of NaOH	No crystallisation even with 300% excess of NaOH
85°	No crystallisation (Poor *S*) [Moderate *S*]	No crystallisation (Poor *S*) [Poor *S*]	No crystallisation even with 300% excess of NaOH	No crystallisation even with 300% excess of NaOH
110°	Good *S* (Good *S*) [Good *S*]	No crystallisation (Good *S*) [Good *S*]	No crystallisation even with 300% excess of NaOH	No crystallisation even with 300% excess of NaOH
150°	No crystallisation (Moderate *B* + *P* and some *S*) [Good *B* + *P*]	Poor *B* (Good *P* and some *B*) [Good *B* + *P*]	No crystallisation (Moderate *P* + some *B*) [Good *P* + some *B*]	No crystallisation (Poor *B*) [Good *B* + some *P*]
200°	Good *B* + *P* (Good *B*) [Good *B*]	Moderate *B* (Moderate *B* + *P*) [Good *B*]	No crystallisation (Good *B*) [Good *B*]	Moderate *B* + some *P* (Good *B*) [Good *B*]
250°	Moderate *B* + *P* (Moderate *B* + *P*) [Moderate *B* + *P*]	Moderate *B* + some *P* (Moderate *B* + *P*) [Good *B* + some *P*]	Poor *B* + *P* (Moderate *B* + *P*) [Moderate *B* + some *P*]	Poor *B* (Poor *B*) [Good *B* + *D*]

small cubic crystals with a maximum size of ~3 μ (Plate 3), isotropic, and having a refractive index of ~1·472. Its range of growth was from gels with $n = \frac{1}{2}$ to $n = 6$ over the range of 60—110°, only 2—3 hr. being required for virtually 100% yields with 200% or 300% excess of sodium hydroxide present at the upper temperature. Under these conditions recrystallisation of species *Q* to species *P* was, however, rapid. At 85° the pattern of species *P* appeared on the *X*-ray photographs only after 5 days' heating of the gel with 300% excess of sodium hydroxide, but at 110° with 200% excess of base conversion into the harmotome-like mineral was complete after 1 day. The recrystallisation could be brought about by treating species *Q* with a normal solution of sodium hydroxide at 100°. In very concentrated gels species *Q* recrystallised to basic sodalite (see species *I* below).

Analysis of species *Q* gave Na_2O, 16·3; Al_2O_3, 28·0; SiO_2, 33·5; H_2O, 22·1%, equivalent to

TABLE 3. *X-Ray data.* d-*Spacings* (Å) *and intensities.**

Species *P*										
Cubic form $a = 10{\cdot}0_1$ Å			Tetragonal form $a = 10{\cdot}0_1$ Å, $c = 9{\cdot}8_8$ Å			Orthorhombic form $a = 14{\cdot}1$ Å, $b = 14{\cdot}0$ Å, $c = 9{\cdot}8$ Å			K-*M* [3]	
hkl	*d*	*I*	*hkl*	*d*	*I*	*hkl*	*d*	*I*	*d*	*I*
—	—	—	—	—	—	001	9·5	m	9·4	mw
—	—	—	—	—	—	101	8·2	mw	8·2	m
110	7·1	s	110	7·1	s	200	7·2	s	7·1	s
—	—	—	—	—	—	020	7·0	mw	7·0	w
—	—	—	111	5·8	vw	201	5·8	mw	5·6	w
—	—	—	—	—	—	211	5·4	w	5·4	m
200	5·0	m	200	5·0	m	220	5·0	s	4·97	m
—	—	—	002	4·94	m	102	4·68	w	4·68	w
—	—	—	102	4·44	vvw	310	4·50	w	4·45	mw
—	—	—	—	—	—	112	4·34	s	4·34	mw
—	—	—	—	—	—	—	—	—	4·28	mw
112	4·10	s	211	4·09	s	311	4·08	s	4·08	mw
—	—	—	112	4·07	vw	—	—	—	—	—
—	—	—	—	—	—	212	3·88	mw	3·86	w
—	—	—	220	3·65	vw	400	3·58	m	3·64	w
220	3·45	vw	202	3·50	vvw	222	3·45	m	—	—
—	—	—	212	3·32	mw	312	3·35	m	—	—
—	—	—	003	3·26	w	013	3·24	m	3·24	vs
310	3·18	vvs	310	3·18	s	420	3·19	vs	3·17	vs
—	—	—	103	3·11	s	—	—	—	—	—
—	—	—	311	3·02	w	—	—	—	—	—
—	—	—	113	2·96	vw	203	2·93	s	2·94	s
222	2·90	vw	—	—	—	—	—	—	2·87	w
—	—	—	203	2·73	vw	223	2·73	m	2·72	mw
321	2·68	s	312	2·68	ms	422	2·68	m	2·67	mw
—	—	—	213	2·65	m	313	2·60	m	2·58	w
400	2·52	vw	400	2·52	w	—	2·51	m	2·48	w
410, 322	2·41	vw	410	2·42	w	—	2·42	vvw	2·42	vw
411, 330	2·36	w	330	2·38	vw	—	—	—	2·38	w
304	2·23	vw	420	2·24	vw	—	2·24	vw	—	—

* s = strong, w = weak, d = diffuse, m = medium, v = very. In certain columns numerals are used, and these are defined as in the original references, the strongest being given as either 10 or 100.

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TABLE 3. (*Continued.*)

Species *S*					K-*G* [8]		Chabazite [33]		Gmelinite [33]	
Hexagonal $a = 13{\cdot}72$ Å $c = 10{\cdot}00$ Å					$a = 13{\cdot}85$ Å $c = 15{\cdot}50$ Å		$a = 13{\cdot}78$ Å $c = 14{\cdot}97$ Å		$a = 13{\cdot}72$ Å $c = 9{\cdot}95$ Å	
hkil	$d_{obs.}$		$d_{calc.}$	*I*	*d*	*I*	*d*	*I*	*d*	*I*
$10\bar{1}0$	11·8		11·9	ms	—	—	—	—	11·9	7
0001	~9·5		10·0	vd	9·5	ms	9·3	7	9·3	6
	—		—	—	—	—	—	—	7·63	4
$11\bar{2}0$	6·85		6·86	s	6·94	m	6·92	3	56·86	4
	—		—	—	—	—	—	—	0·99	1
	—		—	—	5·55	vvw	5·47	6	5·51	4
0002	5·01		5·00	s	5·24	m	4·96	5	5·01	6
	—		—	—	4·78	vvw	—	—	—	—
$21\bar{3}0$	4·46		4·49	mw	—	—	4·60	1	4·58	1
	—		—	—	4·32	s	4·29	8	4·33	5
$30\bar{3}0$	3·962		3·961	mw	3·95	ms	—	—	4·08	5
	—		—	—	—	—	3·82	3	3·85	1
	—		—	—	3·68	mw	3·66	5	3·59	4
$22\bar{4}0$	3·431		3·430	s	3·45	mw	3·39	3	3·40	4
$31\bar{4}0$	3·280		3·296	vvw	—	—	—	—	—	—
$10\bar{1}3$	3·167	{	3·211	vw	3·18	mw	3·187	3	3·209	5
$30\bar{3}2$		{	3·106							
$40\bar{4}0$	2·970		2·971	m	—	—	—	—	—	—
$20\bar{2}3$	2·900		2·908	mw	2·93	vvs	2·907	9	2·912	8
$22\bar{4}2$	2·829		2·828	mw	—	—	—	—	—	—
	—		—	—	—	—	2·675	1	2·683	5
$41\bar{5}0$	2·595		2·593	s	2·59	ms	2·578	4	2·585	4
	—		—	—	—	—	2·431	4	2·495	2
$20\bar{2}4$	2·284		2·305	w	2·29	ms	2·287	2	2·292	2
	—		—	—	2·17	m	—	—	2·201	1
$33\bar{6}3$	2·113	{	2·112	w	2·10	mw	—	—	—	—
$30\bar{3}4$		{	2·116							
$33\bar{6}2$	2·083		2·081	s	2·07	w	2·076	3	2·080	4
	—		—	—	—	—	2·006	1	—	—
$11\bar{2}5$	1·901	{	1·919	m	1·89	vw	1·910	1	1·933	1
$40\bar{4}4$		{	1·915							
	—		—	—	1·84	mw	1·852	2	1·848	1
$41\bar{5}4$	1·800		1·800	s	—	—	1·797	5	1·797	5
4480	1·716		1·715	s	1·72	s	1·716	4	1·716	4
7070	1·687		1·697	m	—	—	—	—	—	—
0006	1·667		1·667	m	—	—	1·675	1	1·669	1
$10\bar{1}6$	1·646	{	1·647	w	—	—	—	—	—	—
6280		{	1·648							
$11\bar{2}6$	1·636		1·620	w	1·64	m	1·631	4	1·631	1

Species *R*					Natural faujasite (Sasbach, Kaiserstuhl)		Species *T*		Nepheline hydrate I [9]		Nepheline hydrate H [9]		Species *Q*				Na-Zeolite. Type *A* [34]	
94·96 † 1 : 2·4 ‡			24·83 † 1 : 3·3 ‡		24·65 † 1 : 4·7 ‡								Cubic $a = 12{\cdot}30$ Å					
hkl	*d*	*I*	*d*	*I*	*d*	*I*	*d*	*I*	*d*	*I*	*d*	*I*	*hkl*	*d*	*I*		*d*	*I*
111	14·52	vs	14·25	vs	14·25	vs	8·2	mw	8·3	ms	—	—	100	12·36	vs		12·294	100
220	8·84	ms	8·75	s	8·70	s	7·6	mw	7·4	ms	—	—	110	8·77	s		8·706	69
311	7·56	ms	7·51	s	7·38	s	—	—	6·4	mw	6·3	mw	111	7·15	s		7·109	35
331	5·74	s	5·71	vs	5·66	vs	5·6	m	5·5	m	5·5	m	200	6·35	w		—	—
511	4·81	m	4·78	m	4·76	s	4·85	w	—	—	—	—	210	5·52	s		5·508	25
440	4·42	ms	4·39	s	4·36	s	4·66	mw	4·72	vvw	4·67	s	211	5·03	w		5·031	2
531	4·20	vvw	—	—	4·16	w	4·46	ms	4·39	vs	4·34	ms	220	4·36	m		4·357	6
620	3·954	w	3·931	m	3·90	w	—	—	4·11	vw	4·07	vs	300, 221	4·102	s		4·107	36
533	3·813	ms	3·789	s	3·76	vs	—	—	—	—	3·84	w	310	3·899	w		—	—
622	3·769	mw	3·746	mw	—	—	—	—	3·61	vw	3·67	vs	311	3·712	s		3·714	53
444	3·621	vvw	3·580	w	—	—	—	—	3·40	vvs	3·40	ms	320	3·413	m		3·417	16
551	3·515	vvw	3·475	w	3·44	w	3·25	m	3·22	vw	3·20	s	321	3·287	ms		3·293	47
642	—§	—	3·321	m	3·29	s(d)	3·17	m	—	—	3·16	w	400	3·072	vw		—	—
731	—	—	3·231	w	3·19	w	2·93	s	2·95	vs	2·95	vvs	410, 322	2·982	vs		2·987	55
733	3·048	m	3·034	mw	3·01	w	2·84	w	2·84	ms	2·84	mw	411, 330	2·900	m		2·904	9
660	2·941	m	2·926	m	2·93	s(d)	2·72	w	—	—	2·74	mw	420	2·751	m		2·754	12
555	2·881	s	2·867	ms	2·81	s	2·58	w	2·60	s	2·59	m	421	2·681	mw		2·688	4
480	2·790	m	2·775	m	2·75	m	2·39	w	2·43	s	2·44	w	332	2·623	s		2·626	22
753	2·745	w	2·729	w	—	—	2·34	w	2·30	vw	2·30	w	422	2·512	mw		2·515	5
842	2·725	vw	2·711	vvw	2·69	w	2·27	w	—	—	2·27	w	430, 500	—	—		2·464	4
664	2·662	m	2·650	m	2·61	m	2·23	w	2·19	mw	2·20	w	431, 510	2·410	w		—	—
931	2·617	mw	2·603	mw	2·58	mw	—	—	2·11	w	2·13	mw	511, 333	2·369	mw		2·371	3
844	2·545	mw	2·534	w	2·51	w	—	—	—	—	2·08	vw	520, 432	—	—		2·289	1
1022	2·403	m	2·391	mw	2·37	ms	2·02	w	2·05	vw	2·04	mw	521	2·247	w		2·249	3
1040	—§	—	—§	—	2·29	w	—	—	1·97	vw	1·97	vw	440	2·174	m		2·177	7
880	2·206	m	2·193	mw	2·17	m	—	—	—	—	1·91	w	441	2·143	mw		2·144	10
955	2·181	m	2·168	mw	2·15	w	1·89	w	1·86	m	1·88	vw	433, 530	2·109	mw		2·113	3
													531	2·078	mw		2·083	4
													600, 442	2·050	m		2·053	9

† Unit cell edge in Å. ‡ Ratio of $Al_2O_3 : SiO_2$.
§ Obscured by lines at 3·343 and 2·282 Å of quartz which was used as an internal standard.

an oxide formula of $Na_2O,Al_2O_3,2{\cdot}0SiO_2,4{\cdot}6H_2O$. The *X*-ray pattern could be indexed to primitive cubic with $a = 12{\cdot}30$ Å (Table 3). An electron-diffraction study by Dr. J. A. Gard showed that this may be a pseudo-cell, the true cell being face-centred cubic with $a \sim 24{\cdot}6$ Å. This conclusion has been firmly established by *X*-ray diffraction [37] by use of the alumino-germanate analogue whose synthesis is here recorded.

[37] Barrer and Meier, *Trans. Faraday Soc.*, 1958, **54**, 1074.

Species *R*, as shown by *X*-ray powder photographs, is a synthetic zeolite related to natural faujasite and to Linde Molecular Sieve X. It was synthesised as very small isotropic crystals (~1 μ) with a cubic crystal habit shown in the electron microphotograph (Plate 4). The refractive index was very difficult to measure but was about 1·46, varying slightly between samples. Its method of preparation varied slightly from that of other species. The concentration of gel used was approximately 1 g. in a total volume of 14 ml. of mixture (with 300% or greater excess of alkali added). About 50 g. of gel were heated in the 1 l. autoclave, stirred at about two revolutions per min. The temperature was raised at ~6° per hr. to between 70° and 80°. This temperature was not critical since some samples were prepared at above 100°. Heating was continued for about two days. The gels used ranged from $n = 1$ to $n = 10$.

The composition of the products varied from $Na_2O,Al_2O_3,2{\cdot}4SiO_2,6{\cdot}7H_2O$ to $Na_2O,Al_2O_3,3{\cdot}3SiO_2,7H_2O$. The cubic face-centred unit cell decreased from 24·96 Å for the most aluminous sample to 24·83 Å at the silica-rich end of the series. This compares with 24·65 Å for a natural faujasite of composition $Na_2O,Al_2O_3,4{\cdot}7SiO_2,9{\cdot}1H_2O$ calculated from an analysis by Damour.[28] *X*-Ray data are in Table 3.

Species *S* was a synthetic sodium analogue of the chabazite–gmelinite natural zeolites. It grew as spherulitic and lenticular crystals with irregular surfaces. These may be aggregates of very tiny crystals. The crystal diameter was usually about 1 μ although one sample was obtained which had crystals of ~12 μ (Plate 5). No birefringence was detected. The refractive index was ~1·458.

This mineral grew from gels $n = 7$ to $n = 10$ and over the range 60—110° with preferably 200% to 300% excess of sodium hydroxide present. The concentration of gel was 1 g. in ~10 ml. of mixture. Best yields were obtained from a gel with $n = 9$ with 300% excess of alkali heated for two days at 100° with continuous vigorous stirring. Analysis of one sample: Na_2O, 10·4; Al_2O_3, 18·1; SiO_2, 54·0; H_2O, 17·5%, which is equivalent to an oxide formula of $Na_2O,Al_2O_3,5{\cdot}1SiO_2,5{\cdot}4H_2O$. *X*-Ray powder data of Table 3 indicated a hexagonal unit cell $a = 13{\cdot}7_2$ Å, $c = 10{\cdot}0_6$ Å.

TABLE 4. *Crystallographic data for* Na-*U*, *rhodesite, and erionite.*

Crystal	Symmetry	Unit-cell dimensions (Å)				Cleavage
Na-*U*	Orthorhombic	Pseudo-cell:	23·5 ± 1·0	6·5	7·0	(100)
	A-centred	True-cell:	23·5 ± 1·0	13·0	14·0	Elongation *C*
Rhodesite	Orthorhombic	Pseudo-cell:	23·8	6·54	7·05	(100)
	A-centred	True-cell:	23·8	13·1	14·1	Elongation *C*
Erionite *	Orthorhombic	Pseudo-cell:	23·0	13·26	7·55	—
	C-centred	True-cell:	23·0	13·26	15·12	Elongation *C*

* The unit cell of erionite is hexagonal, $a = 13{\cdot}26$, $c = 15{\cdot}12$ Å. In the Table the equivalent orthorhombic cell is given.

Species *B* is a zeolite practically identical with natural analcite. It grew as spherulitic and cubic crystals, refractive index ~1·486. The lowest temperature of synthesis was 150°, *i.e.*, it did not grow at temperatures lower than those previously investigated. Its conditions of growth and cation-exchange, chemical, and sorptive properties have been investigated.[2, 6, 7, 29, 30, 31]

Species *D*, synthetic mordenite, has also been investigated fully.[1, 16] It was synthesised as typical wheatsheaf-shaped crystals, but again only in the temperature range observed previously.[1, 16]

Species *U* (Plate 6) was shown optically to grow as needles or fibres from gels with $n = 5$ to $n = 12$ at 250° with 100% to 300% excess of base added. These were usually associated with analcite, but although appearing in some cases to be in almost 20% yield, no reflections other than those due to analcite or the harmotome-like mineral, Na-*P*, were noted on the *X*-ray photographs. However, electron diffraction studies of single crystals by Dr. Gard showed it

[28] Damour, *Ann. Mines*, 1848, **14**, 67.
[29] Barrer, *J.*, 1950, 2342.
[30] *Idem*, *Proc. Roy. Soc.*, 1938, *A*, **167**, 392, 406.
[31] Barrer and Ibbitson, *Trans. Faraday Soc.*, 1944, **40**, 206.

to have an orthorhombic cell resembling that of a new zeolitic silicate mineral, rhodesite.[33] There is also a more superficial resemblance to erionite. These relations are tabulated (Table 4) from information supplied by Dr. Gard. Species *U* is probably of the rhodesite family.

Felspathoids. " Basic " nosean occurred at temperatures of 150° or more from gels with $n = 1$ to $n = 3$ with 100% to 300% excess of alkali. The optical properties, unit-cell dimensions and range of growth have been defined by Barrer and White.[1]

" Basic " sodalite was grown from very concentrated $Na_2O,Al_2O_3,2SiO_2$ gels containing originally 1 g. of gel in 8 ml. of mixture but these were allowed to become more concentrated by evaporation at ~100° (water-bath). Maximum yields were obtained with 300% excess of sodium hydroxide. After about 1 day on the water-bath, lines of species *Q* were also evident on the *X*-ray photograph but after 4—5 days conversion into sodalite was complete. Spherulitic and cubic crystals were observed, of maximum size ~13 μ. The crystals were isotropic, the refractive index varying between 1·468 and 1·493. The unit cell of one sample was calculated as cubic, $a = 8{\cdot}9_4$ Å and analysis [33] showed it to have the composition $Na_2O,Al_2O_3,2{\cdot}1SiO_2,2NaOH,1{\cdot}5H_2O$.

Species *T* only occurred once. It appeared from a gel with $n = 2$ in presence of 300% excess of alkali after being heated for 1 day at 200°. Analcite and nosean were also present, but the *X*-ray powder pattern of species *T* was easily differentiated from these, being closely similar to those of the nepheline hydrate minerals obtained earlier [1] although identical with neither (Table 3). Its temperature of synthesis was lower than that reported for hydrates I and II although the gel composition was similar.

Crystallisation of mixed Na–K *gels.* We first consider the effect of increasing amounts of sodium hydroxide upon the crystallisation for 4 days at 150° of an aqueous gel of composition $K_2O,Al_2O_3,4SiO_2,mH_2O$. The results (Table 5) indicate that the products depend in a striking way on the Na : K ratios, and probably on the $(Na_2 + K_2)O : Al_2O_3$ ratios.

TABLE 5.

Gel composition, excluding H_2O					
Na_2O	K_2O	Al_2O_3	SiO_2	Crystallisation products	
0	1·00	1·00	4·00	K-*G* [3]	(chabazite-type zeolite)
0·286	1·00	1·00	4·00	K, Na-*G*	(chabazite-type zeolite)
0·572	1·00	1·00	4·00	K, Na-*M*	(phillipsite-type zeolite)
0·858	1·00	1·00	4·00	Na, K-*I* *	(sodalite-type phase)
1·716	1·00	1·00	4·00	Na, K-*P*	(harmotome-type zeolite)
1·00	0	1·00	4·00	Na-*B* [3]	(analcite)

* The autoclave leaked during the experiment, and the product was dry.

In a second, more extended series of experiments we investigated the effect of temperature, and of molar proportions of silica, upon the crystallisation processes. In Table 6 the crystalline phases derived from Na-, (Na, K)-, and K-gels are compared, the nomenclature [3] of the relevant potassium minerals being: K-*A*, Sanidine; K-*B*, α-quartz; K-*C*, leucite; K-*F*, K-zeolite; K-*G*, K-zeolite; K-*H*, bayerite; K-*M*, K-zeolite; K-*N*, kalsilite. The phases obtained from mixed gels are classified on the basis of *X*-ray data according as they are structurally related to the potassium phases above, or the sodium phases previously discussed. In a phase such as (K, Na)-*M* the sequence (K, Na)- indicates that *M* refers to the potassium mineral nomenclature. Similarly in (Na, K)-*P* the sequence (Na, K)- indicates that *P* refers to the sodium mineral nomenclature already indicated (Table 1). Crystallisations from homoionic Na-gels refer to the conditions given in Table 2, *i.e.*, to conditions in which additional sodium hydroxide is added so that the ratio $Na_2O : Al_2O_3$ exceeds unity in the aqueous gels. Similarly the homoionic K-gels are those crystallised as described previously [3] from aqueous media containing additional potassium hydroxide. The significance of the description of composition of the mixed gels can be shown by an illustration: in the mixed gel having the ratio $Al_2O_3 : SiO_2 = 1 : 6$, the figures in parentheses (Table 6) associated with Na_2O and K_2O mean that the overall molar proportions of the components were $Na_2O : K_2O : Al_2O_3 : SiO_2 = 1{\cdot}82 : 1{\cdot}00 : 1{\cdot}00 : 6{\cdot}00$, together with about 10 ml. of water. About 0·5 g. of solid gel were crystallised in each experiment.

[33] Barrer and Falconer, *Proc. Roy. Soc.*, 1956, *A*, **236**, 227.
[3] Gard and Taylor, *Mineralog. Mag.*, 1957, **31**, 611.

XUM

Comparison of the results in Table 6 covering the temperatures 60—250° leads to the following conclusions:

(i) There is widespread occurrence of phases related to the phillipsite–harmotome group (Na-*P*, K-*M*), whether from homoionic or mixed gels. In the sodium field, Na-*B*(analcite) is prominent above 150°.

TABLE 6. *Comparison of modes of crystallisation of* Na-, (Na,K)-, *and* K-*gels.*

Temp.	1 : 2 = Al_2O_3 : SiO_2				1 : 3 = Al_2O_3 : SiO_2			
	Na-gel	$Na_2O + K_2O$ (1·03) (2·00)	$Na_2O + K_2O$ (1·00) (2·00)	K-gel	Na-gel	$Na_2O + K_2O$ (1·25) (1·00)		K-gel
60°	Na-*Q*, Na-*P*	(Na, K)-*P*, (K, Na)-*F*	—	K-*G*, K-*H*	Na-*P*, Na-*Q*	—		K-*G*, K-*H*
85	Na-*Q*, Na-*R*	(Na, K)-*P*	—	K-*G*, K-*H*	Na-*P*, Na-*Q*	(K, Na)-*M*		K-*G*, K-*H*
110	Na-*Q*, Na-*P*	(Na, K)-*P*	(Na, K)-*P*	K-*F*	Na-*P*, Na-*Q*	—		K-*F*
150	Na-*F*, Na-*B*	(K, Na)-*G*, (K, Na)-*M*	—	K-*F*	Na-*F*, Na-*B*	(K, Na)-*M*		K-*F*, K-*G*
200	Na-*F*	(K, Na)-*F*	—	K-*M*	Na-*F*, Na-*B*	(Na, K)-*B*		K-*M*
250	Na-*F*, Na-*B*	—	—	K-*M*	Na-F, Na-*B*	(K, Na)-*N*		K-*M*

	1 : 4 = Al_2O_3 : SiO_2				1 : 5 = Al_2O_3 : SiO_2			
	Na-gel	$Na_2O + K_2O$ (1·43) (1·00)	$Na_2O + K_2O$ (1·00) (2·00)	K-gel	Na-gel	$Na_2O + K_2O$ (1·63) (1·00)		K-gel
60	Na-*P*, Na-*Q*	(K, Na)-*M*	—	K-*G*, K-*H*	Na-*Q*, Na-*P*, Na-*R*	(K, Na)-*M*		K-*G*, K-*H*
85	Na-*P*, Na-*Q*	(K, Na)-*M*	—	K-*G*, K-*H*	Na-*Q*, Na-*P*	(K, Na)-*M*		K-*G*, K-*H*
110	Na-*P*, Na-*Q*	(K, Na)-*M*	(Na, K)-*P*	K-*F*	Na-*Q*, Na-*P*	(K, Na)-*M*		K-*F*
150	Na-*B*	(K, Na)-*M*	—	K-*G*	Na-*B*	(K, Na)-*M*		K-*G*
200	Na-*B*	Na-*J*, (Na, K)-*B* or (K, Na)-*N*	—	K-*M*	Na-*B*	(Na, K)-*P*		K-*A*, K-*M*
250	Na-*B*	Na-*J*, (Na, K)-*B* or (K, Na)-*N*	—	K-*M*, K-*C*	Na-*B*	(K, Na)-*A*		K-*A*

	1 : 6 = Al_2O_3 : SiO_2			1 : 7 = Al_2O_3 : SiO_2			
	Na-gel	$Na_2O + K_2O$ (1·82) (1·00)	K-gel	Na-gel	$Na_2O + K_2O$ (2·02) (1·00)	$Na_2O + K_2O$ (1·00) (1·00)	K-gel
60	Na-*P*, Na-*Q*, Na-*R*	(K, Na)-*M*	K-*G*, K-*H*	Na-*P*, Na-*S*, Na-*R*	K-*H*	—	K-*H*, K-*G*
85	Na-*P*, Na-*Q*	(K, Na)-*M*	K-*G*, K-*H*	Na-*P*	K-*H*	—	K-*M*, K-*G*
110	Na-*P*, Na-*Q*	(K, Na)-*M*	K-*G*	Na-*P*	—	(Na, K)-*P*	K-*M*, K-*F*, K-*G*
150	Na-*B*	(K, Na)-*M*	K-*G*	Na-*B*	K-*H*	—	K-*M*
200	Na-*B*	(K, Na)-*M*	K-*A*, K-*M*	Na-*B*	(K, Na)-*A*	—	K-*A*
250	Na-*B*	(Na, K)-*B*, (K, Na)-*M*	K-*A*, K-*M*	Na-*D*, Na-*B*	(K, Na)-*A*	—	K-*A*

	1 : 8 = Al_2O_3 : SiO_2			1 : 9 = Al_2O_3 : SiO_2			
	Na-gel	$Na_2O + K_2O$ (2·22) (1·00)	K-gel	Na-gel	$Na_2O + K_2O$ (2·41) (1·00)		K-gel
60	Na-*P*	K-*H*	K-*H*	Na-*P*, Na-*S*	K-*H*		K-*H*
85	Na-*P*	K-*H*	K-*M*, K-*G*	Na-*P*, Na-*S*	—		K-*H*
110	Na-*P*	—	K-*M*, K-*H*	Na-*P*, Na-*S*	—		K-*H*
150	Na-*B*	—	K-*M*	Na-*B*	K-*H*		K-*M*, K-*H*
200	Na-*B*	(K, Na)-*A*	K-*A*, K-*M*	Na-*D*, Na-*B*	(K, Na)-*A*		K-*A*, K-*M*
250	Na-*B*	—	K-*A*	Na-*B*, Na-*D*	—		K-*A*

	1 : 10 = Al_2O_3 : SiO_2			1 : 12 = Al_2O_3 : SiO_2			
	Na-gel	$Na_2O + K_2O$ (2·61) (1·00)	K-gel	Na-gel	$Na_2O + K_2O$ (3·00) (1·00)		K-gel
60	No crystn.	K-*H*	K-*H*	No crystn.	K-*H*		K-*H*
85	Na-*S*	K-*H*	K-*H*	No crystn.	K-*H*		K-*H*
110	Na-*S*	—	K-*H*	No crystn.	—		K-*H*
150	Na-*S*, Na-*B*, Na-*P*	K-*H*	K-*A*, K-*B*	Na-*B*, Na-*P*	K-*H*		K-*A*, K-*B*
200	Na-*B*, Na-*P*, Na-*D*	(Na, K)-*B*, (K, Na)-*N*	K-*B*, K-*A*	Na-*B*, Na-*P*	(K, Na)-*A*, (K, Na)-*B*		K-*B*, K-*A*
250	Na-*B*, Na-*P*, Na-*D*	—	K-*B*, K-*A*	Na-*B*, Na-*D*	—		K-*B*, K-*A*

(ii) It is sometimes possible to predict the crystals grown from mixed gels from those grown from homoionic gels, *e.g.*, the phases related to the phillipsite–harmotome groups. However, such predictions refer to a situation where mineral-type compounds of this group are grown from both corresponding homoionic gels under like experimental conditions.

(iii) Some Na-phases had no crystalline analogue derived from the corresponding potassium gels, and conversely (*e.g.*, *F*, *I*, *Q*, *R*, and *D* in the Na-species, and *F* and *N* in the K-species). The phases formed from mixed gels are then not readily predictable. Thus phases analogous to Na-*D*, Na-*F*, Na-*I*, Na-*Q*, and Na-*R* were absent from the mixed crystallisates, although analogues of K-*N* and K-*F* were noted and also analogues of Na-*B*. K-*G* (a compound of the chabazite family) was less often formed from the mixed gels than from corresponding K-gels. Na-*S* (also of the chabazite family) did not appear as a product from the mixed gel.

(iv) The frequent occurrence of K-*H* (bayerite, $Al_2O_3,3H_2O$) from K-gels and mixed (Na, K)-gels is considered to be due primarily to the mode of formation of these gels, in all of which freshly prepared aluminium hydroxide was used. The Na-gels on the other hand were made by use of sodium aluminate and silica sol. Thus the mode of preparation of the gel may influence the products.

The foregoing investigation of crystallisation of mixed (Na,K)-gels is adequate as far as the temperature is concerned, up to 250°, but does not cover a wide range of Na : K ratios. It is possible that new products would appear over an increased range in this ratio.

Crystalline phases containing gallium and germanium. Crystallisations were carried out at one temperature, 100°. The crystalline species obtained were:

Gallosilicates	Na-*V*	(Thomsonite-type zeolite)
Aluminogermanates	Na-*R*	(Faujasite-type zeolite)
	Na-*Q*	(Analogue of Linde Sieve A)
	Na-*P* *	(Analogue of harmotome)
Gallogermanates	Na-*V*	
	Na-*R*	
	Na-*I*	(Analogue of basic sodalite)

* By recrystallisation of the Na-*Q*.

Some details of the crystallisation conditions are given in Table 7. Evidently replacement of Al by Ga, or both Al and Si by Ga and Ge, makes easy the synthesis of a zeolite closely related to thomsonite (one of the fibrous zeolites). This zeolite has not been synthesised in the many experiments we have conducted with gels of Li, Na, K, Rb, and Cs. Moreover it is possible to prepare the important molecular-sieve zeolites Na-*R* and Na-*Q* (which are analogous

TABLE 7. *Crystallisation of aluminogermanates, gallosilicates, and gallogermanates at* 100°.

Ratio Al_2O_3 : GeO_2 in gel	Excess of NaOH (mol. %)	Time (hr.)	Products	Ratio Ga_2O_3 : SiO_2 or: GeO_2 in gel	Excess of NaOH (mol. %)	Time (hr.)	Products
Aluminogermanates				*Gallosilicates*			
3 : 2	90	15	Na-*Q*	1 : 0·67	50	26	(Na-*V*) *
1 : 1	125	15	Na-*Q*	1 : 1	50	26	(Na-*V*)
1 : 2	225	15	Na-*Q*	1 : 1·33	50	26	Na-*V*
1 : 3	325	15	Na-*Q*	1 : 2	50	26	Na-*V*
1 : 4	425	15	(Na-*Q*) *	1 : 4	50	26	Na-*V*
1 : 6	625	15	Na-*R*	1 : 4	50	26	Na-*V*
1 : 1	125	40	Na-*R* and Na-*Q*	1 : 5	50	26	Na-*V*
1 : 4	425	40	Na-*R* and Na-*Q*	1 : 6	50	26	Na-*V*
1 : 2	225	7	Na-*Q*				
1 : 6	625	22	Na-*R*	*Gallogermanates*			
1 : 2	225	22	Na-*R* and Na-*Q*	1 : 1	150	40	Na-*R*
1 : 1	125	46	Na-*R*	1 : 1	150	40	Na-*I*
1 : 2	225	46	Na-*R* and (Na-*Q*)	1 : 2	250	40	(Na-*R*)
1 : 2	225	46	Na-*R* and (Na-*Q*)	1 : 2	250	40	(Na-*V*)
1 : 4	425	46	(Na-*R* and Na-*Q*)	1 : 4	450	40	Na-*V*
1 : 1	125	46	Na-*R* and Na-*Q*	1 : 5	550	40	(Na-*V*)
1 : 2	225	46	Na-*R*	1 : 6	650	40	—
1 : 2	225	46	Na-*R*				
1 : 4	425	46	(Na-*R* and Na-*Q*)				
1 : 1	125	31	Na-*R* and Na-*Q*				

* Parentheses indicate minor yields only.

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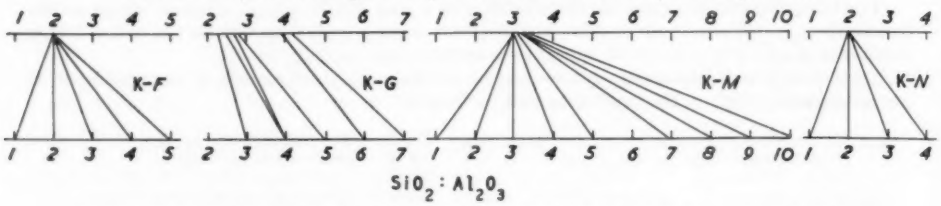
to Linde Molecular Sieves A and X) with Ga replacing all the Al; and in the case of Na-R with full replacement of Al by Ga and of Si by Ge. This full isomorphous replacement by Ga and Ge is likewise found in the very characteristic sodalite-type phase Na-*I*. We thus have phases structurally analogous to certain aluminosilicates, but free from both Al and Si. The important ionic radii are: Al^{3+}, 0·57; Si^{4+}, 0·37; Ga^{3+}, 0·62; Ge^{4+}, 0·44 Å, and differ most for the pair Ga–Si. The unit cells (Å) of the aluminosilicate phases and of those containing Ge or Ga and Ge were measured:

	Al, Si	Al, Ge	Ga, Ge
Na-*I* (sodalite-type)	8·94	—	9·09
Na-*Q* (analogue to Linde Sieve A)	12·30	12·35	—
Na-*R* (analogue to faujasite and Linde Sieve X)	$24{\cdot}8_5$	$25{\cdot}0_0$	$25{\cdot}2_5$

These unit-cell dimensions clearly reflect the different ionic radii, and suggest that the structural tetrahedra SiO_4^{4+}, GeO_4^{4+}, AlO_4^{5-}, and GaO_4^{5-} differ in dimensions. Just as the Al–Si form of Na-*Q* recrystallised readily to Na-*P*, the harmotome-like phase, so also the Al–Ge form of

FIG. 2. *Composition changes when potassium alumino-silicate gels are crystallised.*

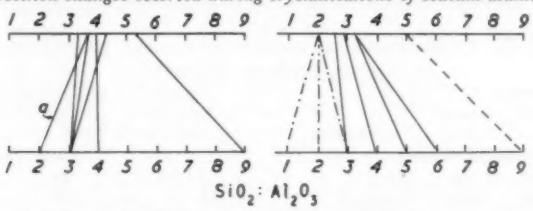


Horizontal scales give values of $SiO_2 : Al_2O_3$ in the parent gels (lower) and products (upper).

Na-*Q* recrystallised to the germanium-containing analogue of Na-*P*. This change could be brought about by treatment of the Na-*Q* for 3 days with N-sodium hydroxide at 100°.

Composition change in crystallisation from gels. In Fig. 2 are shown changes in the ratio $SiO_2 : Al_2O_3$ which occur during the crystallisation of potassium aluminosilicate gels, under conditions described earlier.[3] The crystallisations are of K-*F* (zeolite), K-*G* (chabazite-type

FIG. 3. *Composition changes observed during crystallisations of sodium aluminosilicate gels.*



Horizontal scales give values of $SiO_2 : Al_2O_3$ in mineral (upper) and gel (lower). In the left hand portion the crystallisation product is Na-*P*.
a, Na-*P*, from species *Q* by treatment with N-sodium hydroxide. In the right-hand portion full lines represent species *R*, dashed lines species *S*, and dots and dashes species *Q*.

zeolite), K-*M* (phillipsite-type zeolite), and K-*N* (kalsilite). Fig. 3 shows the changes in $SiO_2 : Al_2O_3 = n$ during crystallisations of sodium aluminosilicate gels (this paper) leading to Na-*P* (harmotome-like zeolite), Na-*R* (faujasite-type zeolite), Na-*Q* (zeolite), and Na-*S* (chabazite-type zeolite).

In the formation of K-*F*, K-*N*, and Na-*Q* from gels of any composition, the $SiO_2 : Al_2O_3$ ratio changes to 2 : 1. For gels yielding K-*G*, the trend is for the crystals to be more aluminous than the gel, and this is true also of K-*M* provided $n > 3$ in the gel, of Na-*R* at least for $3 < n < 6$, and of Na-*S* for $n = 9$. In the case of Na-*P*, gels having $2 < n < 9$ yield crystals with $3{\cdot}3 < n < 5{\cdot}3$. According to Loewenstein's rule,[34] in all aluminosilicates with frameworks

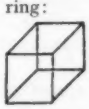
[34] Loewenstein, *Amer. Min.*, 1954, **39**, 92.

built from $(Al,Si)O_4$ tetrahedra, no Al–O–Al bonds can form, and consequently all gels having $n < 2$ must yield more siliceous species, with $n \geqslant 2$. However, if $n > 2$ the larger its value the greater is the tendency of the crystalline phase to be more aluminous than the parent gel.

Discussion

The formation of diverse kinds of structural framework leads to questions as to the mechanism of growth. The phases are often obtained reproducibly in yields nearing 100% and the free-energy balance between the many possible aluminosilicate nuclei must be delicate. The development of elaborate and continued space patterns by progressive additions of single $(Al,Si)O_4$ tetrahedra is difficult to imagine, particularly in the case of very open zeolite structures. The formation of these frameworks is, however, much more easily visualised if in the aqueous crystallising magma there are secondary building units in the form of rings of tetrahedra, or polyhedra. These may pack in various simple co-ordinations to yield different aluminosilicates. Table 8 indicates some possible anions, from which more complex ones can be formed. Thus, appropriate linking of six 4-ring anions can give the cubo-octahedral unit so characteristic of the nosean–sodalite family. It may be considered that the high anionic charges given in Table 8 make the real existence of such complex anions unlikely. However there is no reason why full ionisation should be realised, since the oxygen atoms linked only to one Al or Si atom may not be $-O^-$ groups but may exist partly as un-ionised –OH groups, freely available for condensation-polymerisation, by which mechanism more complex units form.

Table 8. *Some complex aluminosilicate anions.*

Anion type	Compositions possible (Al and Si)	Maximum charge	Total no. of configurations	Anion type	Compositions possible (Al and Si)	Maximum charge	Total no. of configurations
Ring of 3 tetrahedra	0Al,3Si (1) *	−6	2	Double 4-ring:	0Al,8Si (1)	−8	6
	1Al,2Si (1)	−7			1Al,7Si (1)	−9	
Ring of 4 tetrahedra	0Al,4Si (1)	−8	3		2Al,6Si (2)	−10	
	1Al,3Si (1)	−9			3Al,5Si (1)	−11	
	2Al,2Si (1)	−10			4Al,4Si (1)	−12	
Ring of 5 tetrahedra	0Al,5Si (1)	−10	3	Double 6-ring (or three 4-rings):	0Al,12Si (1)	−12	25
	1Al,4Si (1)	−11			1Al,11Si (1)	−13	
	2Al,3Si (1)	−12			2Al,10Si (7) †	−14	
Ring of 6 tetrahedra	0Al,6Si (1)	−12	5		3Al,9Si (8) ‡	−15	
	1Al,5Si (1)	−13			4Al,8Si (6) †	−16	
	2Al,4Si (2)	−14			5Al,7Si (1)	−17	
	3Al,3Si (1)	−15			6Al,6Si (1)	−18	

* Figures in parentheses denote the number of distinguishable configurations of the particular composition given.
† Two pairs of these configurations are non-superposable mirror images.
‡ Three pairs of these configurations are non-superposable mirror images.

In all the zeolites whose structures have been determined, except heulandite,[35] each $(Al,Si)O_4$ tetrahedron is a member of at least one 4-ring. Also, even-numbered rings of 4, 6, 8, or 12 tetrahedra are more usual than odd-numbered rings. This could indicate in part a tendency of Al–O–Si bonds to be preferred to Si–O–Si bonds (cf. Figs. 2 and 3), since structures containing odd-numbered rings must contain Si–O–Si bonds. All zeolites and other framework aluminosilicates having $SiO_2 : Al_2O_3 = 2 : 1$ (and in which therefore only Al–O–Si bonds should occur) should be built only from even-numbered ring units (*e.g.*, Na-*Q*, K-*F*, K-*N*). The more siliceous zeolites could in principle have 5-rings (*e.g.*, heulandite), or other odd-numbered rings, in the structural motif, although not many odd-numbered rings have been recorded.

[35] Ventriglia, *Periodico Miner., Rome*, 1955, **24**, 49.

The frequent occurrence of 4-rings in the structural pattern suggests that this unit leads to very stable patterns. The nucleation of aluminosilicates may in such species be initiated from 4-ring anions. If two of these join together a cubic anion results (Table 8), and these cubes may be stacked in 8-fold co-ordination to give Na-*Q* (Linde Sieve A).[26] It is particularly interesting that this structure may be so visualised, for it can equally well be regarded as formed by an appropriate stacking of cubo-octahedral anions[36] in 6-fold co-ordination. Another mode of arranging the cubic anions of Table 8 in 8-fold co-ordination leads to Na-*P*, K-*M*, and other zeolites of the harmotome–phillipsite group.[34]

Again, if three 4-rings are appropriately linked by oxygen bridges, the double 6-ring anion of Table 8 is formed. The faujasite type of zeolite (faujasite, Na-*R*, Linde Sieve X) then results if these units are joined in six-fold co-ordination. This mode of building the framework is alternative to a four-fold co-ordination of cubo-octahedral units.[37]

Two of us (F. W. B. and J. W. B.) thank the D.S.I.R. for Maintenance Grants, and one of us (W. M. M.) the Schweizerische Nationalfords for an award. We are also indebted to Dr. J. A. Gard for information as quoted.

IMPERIAL COLLEGE, LONDON, S.W.7. [*Received, June 18th*, 1958.]

[34] Barrer, Report on "Physical Chemistry of some Non-Stoicheiometric Phases," 10th Solvay Council, Brussels, May 1956, p. 21.
[37] Barrer, Bultitude, and Sutherland, *Trans. Faraday Soc.*, 1957, **53**, 1111.

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37. *Heterocyclic Imines and Amines. Part IX.* Glutarimidine and the Imidine from α-Phenylglutaronitrile.*

By J. A. ELVIDGE, R. P. LINSTEAD, and ANN M. SALAMAN.

Addition of ammonia to glutaronitrile gives the 6-membered ring compound, glutarimidine (II). This, like succinimidine, has two reactive imino-groups which undergo displacement reactions with water, hydroxylamine, and aniline.

There are apparently errors in early work by Biedermann on products from glutaronitrile and hydroxylamine.

α-Phenylglutaronitrile with ammonia yields the analogous α-phenylglutarimidine (XII), which condenses with aniline and hydroxylamine, the latter yielding the dioxime (XIII). This was degraded to α-phenylglutarimide, in turn synthesised from α-phenylglutaric acid.

Light absorptions are given (and revised for some succinimidine derivatives) and fine structures are discussed. The glutarimidines show no great readiness to undergo dehydrogenation, and are regarded as di-imino- or amino-imino-piperidines, not as diaminodihydropyridines.

THE imidines described in previous papers [1-4] were 5-membered-ring compounds, prepared by addition of ammonia to 1 : 2-dinitriles. We have now obtained imidines with 6-membered rings, as readily, from the 1 : 3-dinitriles glutaronitrile and α-phenylglutaronitrile.

Glutarimidine.—Glutaronitrile (I) with methanolic ammonia at 100° afforded crystalline glutarimidine† (II), $C_5H_9N_3$, characterised as the picrate. The cyclic imidine structure (II) for the new base was indicated by its reactions and confirmed by infrared spectroscopy which showed the absence of a nitrile group (see Table 1, p. 210). Neither the base nor

* Part VIII, *J.*, 1957, 709.
† Concerning nomenclature, see *J.*, 1954, 442.

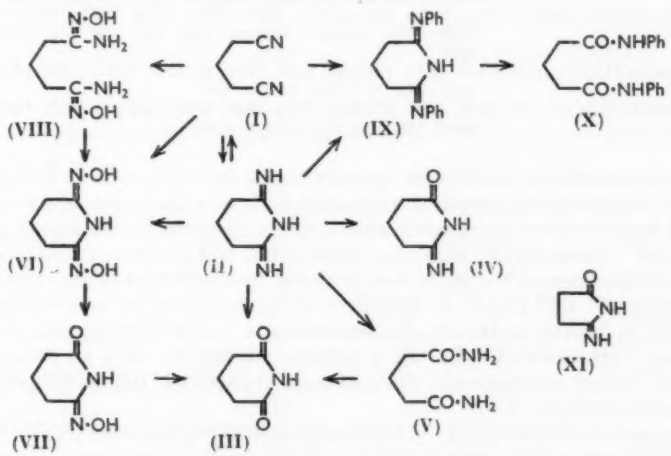
[1] Elvidge and Linstead, *J.*, 1952, 5000.
[2] *Idem*, *J.*, 1954, 442.
[3] Ficken and Linstead, *J.*, 1955, 3525.
[4] Linstead and Whalley, *ibid.*, p. 3530.

a salt has been described before, although Pinner [5] apparently obtained a molecular compound of the hydrochloride with glutardiamidine dihydrochloride from the reaction of di*iso*butyl glutardi-imidate with ammonia.

Glutarimidine was unstable to heat, and in boiling butanol dissociated into glutaronitrile (I) and ammonia. Analogous reversal of imidine formation occurred [6] on strong heating of di-imino*iso*indoline, which gave phthalonitrile and ammonia.

Glutarimidine resembled succinimidine [2] in being readily hydrolysed but there was a difference in that stepwise control of the hydrolysis was not easily achieved. On exposure of glutarimidine to moist air, ammonia and a mixture of solids were formed. Treatment of glutarimidine with cold water also gave a mixture, from which we isolated glutarimide (III). An intermediate hydrolysis product, the imino-imide (IV), was obtained when an ethanolic-toluene solution of the imidine was, by chance, exposed to the atmosphere for some days. The cyclic structure (IV) which is isomeric with glutaric cyano-amide [7] was confirmed by the infrared absorption (Table 1) which showed no nitrile stretching and a general similarity to that of iminosuccinimide (XI). After treatment of glutarimidine with boiling water, sparingly-soluble glutaramide (V) was isolated, the hydrolysis under these conditions having taken a different course, as discussed below.

Glutarimidine (II) condensed with 2 molecular proportions of hydroxylamine hydrochloride in boiling ethanol, as expected: [2] the cyclic dioxime structure (VI) for the product was confirmed by successive conversion with nitrous acid into the monoxime [8] (VII), and thence into glutarimide (III). The cyclic dioxime (VI) was also formed from glutaronitrile and 2 mols. of hydroxylamine at 90°. From glutaronitrile and hydroxylamine at 60—70°, the acyclic bisamidoxime (VIII) was obtained in low yield. This product showed a double melting point which suggested that it cyclised on heating: indeed, sublimation converted it smoothly into the cyclic dioxime (VI).



These inter-relations make the structures (VI), (VII), and (VIII) certain. We believe therefore that there are errors in a paper by Biedermann,[9] describing products from glutaronitrile and hydroxylamine. The melting points that he gave for compounds assigned structures (VIII) and (VI) are very different from ours. Moreover, he obtained his bisamidoxime (VIII) as a hydrate whereas, without precautions, our product (VIII) was

[5] Pinner, *Ber.*, 1890, **23**, 2942.
[6] Elvidge and Linstead, *J.*, 1955, 3536.
[7] Beilstein, " Handbuch der Organischen Chemie," 4th edn., H **2**, 634.
[8] Garny, *Ber.*, 1891, **24**, 3426.
[9] Biedermann, *Ber.*, 1889, **22**, 2967.

obtained anhydrous. That his " bisamidoxime " had perhaps been nadvertently converted into the cyclic dioxime (VI), as the melting point suggests, is supported by Garny's conversion [8] of it with 1 mol. of nitrous acid into the cyclic monoxime (VII).

Attempts to condense glutarimidine with 2-aminopyridine, 2 : 6-diaminopyridine, and di-imino*iso*indoline were abortive. However, condensation with aniline readily gave the diphenylimino-derivative (IX). The same compound (IX) was also obtained in good yield by basification of a hydrochloride produced by melting aniline hydrochloride with glutaronitrile. This last route to an *NN'*-diphenyl-imidine derivative had earlier been successful with succino- and phthalo-nitrile,[2] but had failed with αα'-dimethylsuccinonitrile.[4]

Hydrolysis of the diphenylimino-compound (IX) with boiling water yielded glutardianilide (X), a result analogous to the production of succindianilide from 2 : 5-diphenyliminopyrrolidine.[2] The hydrolysis also recalls that of glutarimidine to glutaramide, mentioned above. It is conceivable that the hydrolysis of an imidine [and derivatives such as (IX)] proceeds by ring opening to an amidino-amide and reclosure: there is, then, the possibility at 100°, that hydrolysis of the transient intermediate amidine will be faster than reclosure of the ring. In that event, diamide is formed, rather than imino-imide (and thence imide).

α-*Phenylglutarimidine* (2 : 6-*Di-imino*-3-*phenylpiperidine*).—α-Phenylglutaronitrile, readily available from benzyl cyanide and acrylonitrile,[10] reacted smoothly with ammonia in methanol at 80° to provide the new imidine (XII). Its infrared absorption, apart from phenyl vibrations, was similar to that of glutarimidine (see Table 1).

TABLE 1. *Infrared absorption* (*Nujol mulls*).

Compound	Principal max. (cm.$^{-1}$)
Glutarimidine (II)	Broad NH absorption; 1688, 1603, 1559, 1414, 1332, 1310, 1217, 1186, 1145, 1087, 1057(w), 966, 918, 910, 885, 758(w), 724(w).
α-Phenylglutarimidine (XII)	Broad NH absorption; 1674, 1600, 1534, 1335, 1292(w), 1284, 1258, 1220, 1100, 1070(w), 1039(w), 991, 930, 908, 876, 769, 750, 724(w), 699.
Iminoglutarimide (IV)	3145, 3072, 1816(w), 1697, 1661, 1531(w), 1332, 1266, 1255, 1176, 1143, 1052, 918, 813, 759, 723(w), 670.
Iminosuccinimide (XI)	3175, 3106, 1767(w), 1681, 1621, 1520, 1339(w), 1290, 1247, 1215, 1152, 1005, 926, 825, 762, 722(w), 676.

α-Phenylglutarimidine (XII) with hydroxylamine hydrochloride in boiling methanol yielded the dioxime (XIII), which was obtained both as a methanol solvate and solvent-free. Mild degradation of the dioxime with nitrous acid afforded a monoxime, presumably the " hindered " isomer (XIV), whilst hot dilute nitric acid smoothly gave the imide (XV). An authentic specimen of the imide was prepared by distillation of the ammonium salt of α-phenylglutaric acid (XVI), in turn derived by hydrolysis of α-phenylglutaronitrile. With aniline in boiling methanol, the imidine gave a monophenylimine, assigned the " unhindered " structure (XVII). At a higher temperature, with an excess of boiling aniline, the second imino-group was replaced, 3-phenyl-2 : 6-diphenyliminopiperidine (XVIII) being obtained.

Structure and Light Absorption.—The di-iminopiperidine structures (XX), (XXa) given to the foregoing compounds accounted satisfactorily for their reactions. Nevertheless, as for succinimidine,[2] the possibility of tautomerism to the amino-imino- (XXI) and diamino-forms (XXII) warranted consideration.

Tautomerism to the diamino-structure (XXII) could be rejected for the present system. This structure is formally a dihydropyridine, so that if tautomerism to this were real the compounds would be expected to be unstable and to undergo dehydrogenation to 2 : 6-diaminopyridine derivatives easily. But the compounds [even the favourable derivative (XVIII)] were rather stable. Moreover, α-phenylglutarimidine and its derivatives and the corresponding glutaric compounds have similar light absorptions (Table 2). This

[10] Koelsch, *J. Amer. Chem. Soc.*, 1943, **65**, 437.

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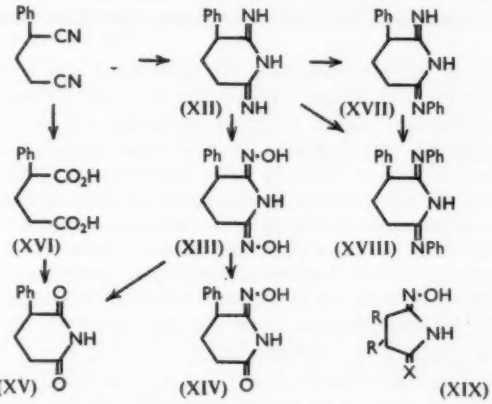
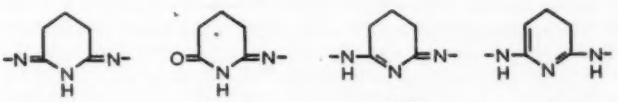
shows that the α-phenyl group is not conjugated with the nitrogenous chromophore, and therefore that the form (XXII) makes no contribution to the structure of these compounds.



It was argued previously [2] that the diene system (XXI) would be expected to absorb light strongly in the 300 mμ region. Consequently it is concluded that the *N*-phenylglutarimidine and -α-phenylglutarimidine derivatives (IX), (XVII), and (XVIII), which



have maxima at approximately 290 mμ (Table 2), like the corresponding succinimidine derivatives,[2,3,4] probably exist in the di-imino-form (XX), but more evidence is being sought on this point.

TABLE 2. *Light absorptions (in ethanol, except as indicated).*

Compound	$\lambda_{max.}$ (mμ)	$10^{-3}\varepsilon$	Compound	$\lambda_{max.}$ (mμ)	$10^{-3}\varepsilon$
Glutarimidine (II)	252	17·2	Monoxime (XIX; R = R′ = H, X = O) [e]	220	13·0
Imino-imide (IV)	239	9·6	Dioxime (XIX; R = R′ = H, X = N·OH) [e]	228	13·3
Glutarimide (III) [a]	198	13·3 [12]	Monoxime (XIX; orientation probably [11] R = Me, R′ = H, X = O) [d]	221	10·0
Dioxime (VI)	234	18·8	Dioxime (XIX; R = Me, R′ = H, X = N·OH)	228	18·1
Monoxime (VII)	226	11·0	Monoxime (XIX; R = R′ = Me, X = O) [e]	221·5	10·5
Diphenylimine (IX)	228, 291	15·8, 11·8	Monoxime (XIX; R = R′ = ·[CH$_2$]$_4$·, X = O) [f]	221·5	10·4
α-Phenylglutarimidine (XII)	256	18·0			
α-Phenylglutarimide (XV) [b]	188, 201 *	51·2, 23·0			
Dioxime (XIII)	238	19·0			
Monoxime (XIV)	217,* 229	11·2, 9·4			
Phenylimine (XVII)	258, 290	15·8, 9·2			
Diphenylimine (XVIII)	227, 288	32·8, 9·75			
Succinimide [c]	191	15·4 [13]			

* Inflexion.
[a] In MeCN. } These measurements were very kindly made by Dr. D. W. Turner of
[b] In 50 : 1 hexane–MeCN. } this Department.
[c] In MeOH; revised data, correcting that in ref. 1.
Correction to data in (*d*) ref. 11, (*e*) ref. 4, *f* (ref. 3).

The tautomeric structure (XXI) is formally a tetrahydropyridine, but it should be reasonably resistant to dehydrogenation because aromatisation to a diaminopyridine could occur only by rearrangement. In fact, dehydrogenation did not accompany the reactions

of the glutarimidines (II) and (XII) with aniline at its boiling point. This behaviour contrasts with that of the substituted succinimidines, *cis*-hexahydrophthalimidine [3] and αα′-dimethylsuccinimidine,[4] which both yield maleimidine derivatives when condensed with aniline under mild conditions, but the dehydrogenation here does not necessitate rearrangement.

A salient feature of glutarimidine and its hydrolysis and hydroxylamine reaction products is their absorption at longer wavelengths than the corresponding succinimidine derivatives,[2,3,4,11] (Table 2). (Initial apparent anomalies led to the redetermination of the spectra of the succinic compounds. Revised data, obtained with a Perkin-Elmer Spectracord 4000, are included in Table 2.) The bathochromic shift for glutarimidine was taken at first to signify a contribution to the structure from the amino-imino-tautomer (XXI). However, tautomerism could hardly be invoked to explain the shift between the oximes in the glutaric series (VI) and (VII) and those in the succinic series (XIX). None of these derivatives shows hydroxylamine character (*i.e.*, instability, ready oxidation) and they all are certainly best represented as having the fixed hydroxyimino-structures of types (XX) and (XIX). It appeared therefore that the shifts were related to the change in ring size between the glutaric and the succinic series. Indeed, this is the basis of Turner's explanation [12] for the longer-wavelength absorption of glutarimide over succinimide. With the expansion in ring size there is no longer coplanarity within the imide group because the carbonyl groups are now twisted about the CO–N linkages. This change in conformation both increases the energy of the ground state and decreases that of the excited state, thus reducing the excitation energy, for an $N \longrightarrow V$ transition of the –CO–NH– chromophore. If the absorption bands for the (structurally closely related) imines and derived oximes and imino-imides arise also from $N \longrightarrow V$ transitions of the analogous –C(:NR)–NH– chromophores (where R = H, OH), then there should be shifts to longer wavelengths on passing from the succinic compounds to the corresponding glutarimidine derivatives. This is observed, and moreover the various shifts are of roughly equal energies, as would be expected. Thus the 15 mμ shift for the imidines represents a decrease in excitation energy of 6·5 kcal./mole,[13] which is of the same order as the energy equivalent of the 7 mμ shift for the imides, namely 5·5 kcal./mole. It is concluded therefore that the glutarimidines (II) and (XII) and their transformation products (IV), (VI), (VII), (XIII), and (XIV) are probably best represented by the di-imino-piperidine structures (XX), (XXa).

The dioxime in the monomethylsuccinimidine series (XIX; R = Me, R′ = H, X = N·OH), data for which are included in Table 2, was prepared from monomethylsuccinonitrile [11] and hydroxylamine.

Experimental

Analyses were by the staff of the Microanalytical Laboratory (Miss J. Cuckney), and measurements of infrared absorption by Mr. R. L. Erskine, B.Sc., and of near-ultraviolet light absorption by Mrs. A. I. Boston of this Department.

Glutarimidine (2 : 6-*Di-iminopiperidine*) (II).—Liquid ammonia (100 c.c.) was added cautiously to methanol (300 c.c.; dried by fractionation) and the solution heated with glutaronitrile [14] (50 c.c., 47·6 g.; $n_D^{19\cdot5}$ 1·4362) in an autoclave at 100° overnight. Evaporation of the solution afforded *glutarimidine* (25·1 g., 45%), which crystallised from dimethylformamide–benzene as prismatic needles, m. p. 157—158° (decomp.) (Found: C, 53·6; H, 8·2; N, 38·0. $C_5H_9N_3$ requires C, 54·0; H, 8·2; N, 37·8%).

The *picrate*, prepared in ethanol, recrystallised from ethanol as yellow prisms, m. p. 210—211° (decomp.) (Found: C, 39·2; H, 4·0; N, 24·4. $C_{11}H_{12}O_7N_6$ requires C, 38·8; H, 3·6; N, 24·7%).

[11] Brown, Spiers, and Whalley, *J.*, 1957, 2882.
[12] Turner, *ibid.*, p. 4555.
[13] Bowen, "Chemical Aspects of Light," Oxford, 1942, p. 188.
[14] *Org. Synth.*, Coll. Vol. I, p. 536.

XUM

Action of Heat.—Glutarimidine (2 g.) evolved ammonia slowly when boiled in butanol (20 c.c.). After 18 hr., the solution was evaporated and the oily residue taken up in benzene and chromatographed on alumina. Elution of the yellow band, with benzene, evaporation of the eluate, and distillation of the residue under reduced pressure afforded glutaronitrile (1·16 g., 69%), b. p. 81°/0·15 mm., n_D^{19} 1·4368.

Hydrolyses.—(i) Glutarimidine was exposed to the atmosphere until ammonia evolution ceased. After being crystallised from ethanol–toluene, the solid (*A*) had m. p. 137—180°. Further fractionation from methanol–benzene, eventually gave a solid (*B*), m. p. 150—160°. These m. p. ranges were unaffected by admixture of *A* with the imino-imide (IV) described below, and of *B* with glutarimide. A mixture of the imino-imide (IV) and glutarimide had the depressed m. p. 137—150°.

(ii) A solution of glutarimidine in a minimum of cold water was kept at 0° for 24 hr. during which ammonia was evolved. Evaporation of a portion of the solution left a solid, m. p. *ca.* 160—200°, which was not separated into its constituents by crystallisation from ethanol and methanol–benzene. Ether-extraction of the remainder of the aqueous hydrolysate for 24 hr. and evaporation of the extract yielded crude glutarimide, m. p. 144—147° and mixed m. p. 145—150° with authentic glutarimide, m. p. 154—155°, prepared by distillation of glutaramide and crystallisation of the distillate from ethyl acetate–light petroleum (b. p. 40—60°).

(iii) Glutarimidine was dissolved in hot toluene by addition of ethanol. After several days, 6-*imino*-2-*piperidone* (IV) had crystallised as plates, m. p. 181—182° (decomp.) (Found: C, 53·9; H, 7·5; N, 24·8. $C_5H_8ON_2$ requires C, 53·6; H, 7·2; N, 25·0%).

(iv) Glutarimidine (2 g.) was boiled with water (2 c.c.) for 1·5 hr. and the solution then kept at 0° overnight. Glutaramide (V) (1·56 g., 42%) separated as leaflets, m. p. 180—181° raised on recrystallisation from water (charcoal) to 182—183° (Found: C, 46·2; H, 7·9; N, 21·1. Calc. for $C_5H_{10}O_2N_2$: C, 46·1; H, 7·8; N, 21·5%). Authentic glutaramide (mixed m. p. undepressed), obtained from dimethyl glutarate and concentrated aqueous methanolic ammonia, crystallised from ethanol as shining plates, m. p. 181—182°. Earlier workers [7] gave m. p.s 175, 176°.

2 : 6-*Dihydroxyiminopiperidine* (VI).—(a) *Preparation.* (i) Glutarimidine (2 g.) and hydroxylamine hydrochloride (2·6 g., 2 mols.) were boiled together in methanol (30 c.c.) for 1·5 hr. Cooling of the solution gave 2 : 6-*dihydroxyiminopiperidine* (1·2 g., 47%), m. p. 231—232° (decomp.), which after crystallisation (3 times) from water, formed prisms, m. p. 240—241° (decomp.) (Found: C, 42·0; H, 6·5; N, 29·5. $C_5H_9O_2N_3$ requires C, 42·0; H, 6·3; N, 29·4%). The compound in aqueous ethanol gave a red-violet colour with ferric chloride and a yellow-green with cupric acetate. (ii) Glutaronitrile (5 g.), hydroxylamine hydrochloride (9·4 g., 2 mols.), and sodium carbonate (7·2 g.) were kept in 50% aqueous ethanol (20 c.c.) at 90° overnight. The clarified solution was evaporated to dryness and the residue extracted with boiling water. Cooling of the extract afforded the dioxime (4·6 g.), m. p. 233—234° and mixed m. p. 234—235°.

(b) *Degradation.* (i) The dioxime (VI) (2 g.) was dissolved in a mixture of 50% aqueous ethanol (10 c.c.) and dioxan (10 c.c.), and 10% sodium nitrite solution (4·83 c.c.) was added. To the stirred solution, 10% hydrochloric acid (2·2 c.c.) was added during 1 hr. Next day, the solution was evaporated to dryness and the residue extracted with boiling ethanol. Concentration of the extract afforded 6-hydroxyimino-2-piperidone (VII) (0·24 g., 28%), m. p. 199—201°, which crystallised from ethanol as prisms, m. p. 201—202° (Found: C, 47·3; H, 6·6; N, 21·6. Calc. for $C_5H_8O_2N_2$: C, 46·9; H, 6·3; N, 21·9%). Garny [8] reported m. p. 196°. The compound in aqueous ethanol gave a faint purple-red colour with ferric chloride and a bright green with cupric acetate. (ii) To this monoxime (VII) (0·2 g.), dissolved in acetic acid (10 c.c.), concentrated hydrochloric acid (0·31 c.c.) was added, followed by 10% aqueous sodium nitrite (1·08 c.c.) in drops. Next day the solution was evaporated, the residue extracted with ethanol, and the extract evaporated. Crystallisation of the solid, m. p. 150—152°, from a minimum of water gave glutarimide as plates, m. p. 153—154° (Found: N, 12·75. Calc. for $C_5H_7O_2N$: N, 12·4%), which did not depress the m. p. of the authentic specimen (above).

Glutardiamidoxime (VIII).—(a) *Preparation.* A solution of glutaronitrile (5 g.), hydroxylamine hydrochloride (4·7 g.), and sodium carbonate (3·6 g.) in 50% aqueous ethanol (20 c.c.) was kept at 60° for 16 hr. The solution was evaporated under reduced pressure and the residue extracted with ethanol. Cooling of the extract gave *glutardiamidoxime* (2·3 g., 27%) which crystallised from ethanol as tiny plates, m. p. 164—165° (with evolution of gas, resolidification, and decomp. at *ca.* 220°) (Found: C, 37·7; H, 7·6; N, 34·7. $C_5H_{12}O_2N_4$ requires C, 37·5;

XUM

H, 7·6; N, 35·0%). The compound in water gave an orange colour with ferric chloride and a dull yellow with cupric acetate.

(b) *Cyclisation.* Sublimation of the preceding diamidoxime at 150°/10 mm. and crystallisation of the sublimate from water afforded the cyclic dioxime (VI), m. p. 228—230° undepressed by that prepared from glutarimidine and hydroxylamine, above.

2 : 6-*Diphenyliminopiperidine* (IX).—(a) *Preparation.* (i) A solution of glutarimidine (2 g.) and aniline (3·4 g.) in ethanol (20 c.c.) was boiled for 18 hr. (ammonia evolved), and then evaporated under reduced pressure. The residue was chromatographed in benzene on a column (14 × 1 cm.) of alumina (Spence type H), the eluate was evaporated, and the gummy product covered with light petroleum (b. p. 40—60°) and kept at 0°. By next day crystallisation had occurred. From ethyl acetate (charcoal), the **2 : 6-*diphenyliminopiperidine*** (3·6 g., 76%) formed colourless prisms, m. p. 153° (Found: C, 77·4; H, 6·7; N, 16·0. $C_{17}H_{17}N_3$ requires C, 77·5; H, 6·5; N, 16·0%).

(ii) Glutaronitrile (5·1 g.) and aniline hydrochloride (14 g.) were mixed together and heated in an oil-bath at 230°. At *ca.* 200° (internal temperature) an exothermic reaction set in, with a rise in temperature to 280°. When the melt had partly solidified, the oil-bath was removed, and subsequently the orange solid was triturated with water, collected, and dried (yield, 11·3 g.; m. p. 255—265°). Crystallisation from ethanol (charcoal) afforded **2 : 6-*diphenyliminopiperidine hydrochloride***, m. p. 274—275° (decomp.) (Found: C, 68·2; H, 6·2; N, 13·9; Cl, 12·0. $C_{17}H_{18}N_3Cl$ requires C, 68·1; H, 6·0; N, 14·0; Cl, 11·8%). The hydrochloride (7 g.) was stirred with 50% aqueous ethanol (80 c.c.) whilst N-sodium hydroxide (23·4 c.c.) was added, followed by water (200 c.c.). Extraction of the solution with chloroform, evaporation of the extract, and treatment of the residue with dry ether gave 2 : 6-diphenyliminopiperidine (6 g.), m. p. and mixed m. p. 152—153°.

(b) *Hydrolysis.* The diphenylimine (0·5 g.), dissolved in dioxan (15 c.c.), was boiled with water (25 c.c.) overnight. On cooling of the solution, glutardianilide separated (0·5 g.), which crystallised from dioxan as needles, m. p. 224° (Found: N, 10·1. Calc. for $C_{17}H_{18}O_2N_2$: N, 9·9%). Barnicoat [15] gives m. p. 223°.

α-*Phenylglutarimidine* (**2 : 6-*Di-imino*-3-*phenylpiperidine***) (XII).—α-Phenylglutaronitrile [10] (48·3 g.) and a solution of liquid ammonia (100 c.c.) in methanol (300 c.c.) were heated in an autoclave at 80° for 18 hr. The solid product (27·9 g.) was crystallised from ethanol to yield **α-*phenylglutarimidine*** as plates, m. p. 201—202° (decomp.) (Found: C, 70·3; H, 7·1; N, 22·3. $C_{11}H_{13}N_3$ requires C, 70·6; H, 7·0; N, 22·4%).

2 : 6-*Dihydroxyimino*-3-*phenylpiperidine* (XIII).—(a) *Preparation.* α-Phenylglutarimidine (2 g.) and hydroxylamine hydrochloride (1·5 g.) were boiled together in ethanol (20 c.c.) for 2·5 hr. during which ammonium chloride separated. The solvent was evaporated under reduced pressure, and the residue was triturated with water. From methanol the product (1·9 g.) crystallised as the *methanol solvate*, m. p. 226—227° (decomp.) (Found: C, 57·2; H, 6·9; N, 16·9. $C_{11}H_{13}O_2N_3,CH_3{\cdot}OH$ requires C, 57·4; H, 6·8; N, 16·7%), which was dried at 120°/18 mm. for 1·5 hr. to yield the solvent-free **2 : 6-*dihydroxyimino*-3-*phenylpiperidine***, m. p. unchanged (Found: C, 60·3; H, 6·2; N, 19·05. $C_{11}H_{13}O_2N_3$ requires C, 60·3; H, 6·0; N, 19·2%). The compound in methanol gave a dark red colour with ferric chloride.

(b) *Degradation.* (i) To the preceding dioxime (0·3 g.) in dioxan (10 c.c.), water (10 c.c.) was added, followed by sodium nitrite (0·2 g.) and then, with ice-cooling, 2N-hydrochloric acid (2 c.c.) in drops. After 15 min., the solution was evaporated under reduced pressure and the residue extracted with ethanol (2 × 20 c.c.). Evaporation of the extract left an oil, which solidified on being triturated with water [yield, 0·19 g.; m. p. *ca.* 200° (decomp.)]. Several crystallisations from ethanol–water (charcoal) yielded **2-*hydroxyimino*-3-*phenyl*-6-*piperidone*** (XIV) as prisms, m. p. 225—226° (decomp.) (Found: C, 64·6; H, 6·2; N, 13·6. $C_{11}H_{12}O_2N_2$ requires C, 64·7; H, 5·9; N, 13·7%). The compound gave a pale orange colour with ferric chloride.

(ii) The dioxime (XIII) (0·5 g.) was warmed on the steam-bath with 2N-nitric acid (10 c.c.). Initially, there was effervescence. After 50 min., ethanol was added, and the solution was evaporated under reduced pressure, and again after addition of ethanol and benzene. The resulting viscous syrup was dissolved in a little ethanol. At 0°, needle-shaped crystals separated (147 mg.), m. p. 138—140°, followed by a further crop (84 mg.), m. p. 135—160°, from the mother-liquors. From benzene, with rejection of insoluble matter and by addition of ether,

[15] Barnicoat, *J.*, 1927, 2926.

XUM

α-phenylglutarimide (167 mg.) was obtained as needles, m. p. 143° undepressed by the authentic material, next described.

α-*Phenylglutarimide* (XV).—α-Phenylglutaronitrile (10 g.) was hydrolysed with a boiling solution of sodium hydroxide (10 g.) in water (30 c.c.) and ethanol (15 c.c.) for 1·5 hr., the mixture (sodium salt had separated) was then acidified with hydrochloric acid and extracted with ether, and the ether was evaporated. Exposure of the syrup as a thin layer to the air gave crude acid, m. p. 65—67°, which was pressed between porous tiles for several days. The α-phenylglutaric acid then had m. p. 80° (Equiv. by titration, 109. Calc. for $C_{11}H_{12}O_4$: equiv., 104). Fichter and Merckens [14] give m. p. 82—83°. The acid in ether (200 c.c.) was converted with ethereal ammonia into ammonium α-phenylglutarate (10·2 g.), distillation of which at atmospheric pressure gave the crude imide, m. p. 130—133° raised to 138—139° on crystallisation from methanol (yield 2·2 g.). From ethyl acetate–ether, α-*phenylglutarimide* formed needles, m. p. 142—143° (Found: C, 70·0; H, 6·2; N, 7·5. $C_{11}H_{11}O_2N$ requires C, 69·8; H, 5·9; N, 7·4%).

2-*Imino*-3-*phenyl*-6-*phenyliminopiperidine* (XVII).—α-Phenylglutarimidine (1 g.) and aniline (1 c.c.; 1 mol.) were boiled in ethanol (20 c.c.) for 24 hr. Evaporation of the solution and trituration of the residue with ether and then ethyl acetate yielded 2-*imino*-3-*phenyl*-6-*phenyliminopiperidine* (1·3 g., 92%) which crystallised from ethanol–water as plates, m. p. 169—170° (decomp.) (Found: C, 77·4; H, 6·7; N, 15·8. $C_{17}H_{17}N_3$ requires C, 77·5; H, 6·5; N, 16·0%).

3-*Phenyl*-2 : 6-*diphenyliminopiperidine* (XVIII).—(i) α-Phenylglutarimidine (2 g.) was boiled in aniline (20 c.c., freshly distilled) overnight and the aniline was then removed at 100°/0·2 mm. The residue crystallised from ethanol, to give pale orange-yellow laths of 3-*phenyl*-2 : 6-*diphenyliminopiperidine* (2·2 g.), m. p. 163° (Found: C, 81·6; H, 6·2; N, 12·4. $C_{23}H_{21}N_3$ requires C, 81·4; H, 6·2; N, 12·4%), whilst from aqueous ethanol the yellow *hemihydrate* separated as very small plates, m. p. 163° (with softening at 149—150°) (Found: C, 79·0; H, 6·25; N, 11·7. $C_{23}H_{21}N_3,\frac{1}{2}H_2O$ requires C, 79·2; H, 6·4; N, 12·0%).

(ii) The diphenylimino-compound (0·1 g.), mixed m. p. undepressed, was isolated similarly after interaction of the monophenylimine (XVII) (0·2 g.) with boiling aniline (1 c.c.) overnight.

Attempts at Dehydrogenation.—No evidence for the formation of substituted diaminopyridines was obtained in preliminary attempts to dehydrogenate 2 : 6-diphenyliminopiperidine (IX), α-phenylglutarimidine (XII) and 3-phenyl-2 : 6-diphenyliminopiperidine (XVIII) by distillation, by heating them in solvents with palladised charcoal and by treatment with chloranil or tetrachloro-*o*-benzoquinone.

2 : 5-*Dihydroxyimino*-3-*methylpyrrolidine* (XIX; R = Me, R′ = H, X = N·OH).—Hydroxylamine hydrochloride (1·6 g.) was dissolved in hot ethanol (50 c.c.) containing methylsuccinonitrile [11] (1 g.), sodium carbonate (1·2 g.) was added cautiously, and the mixture boiled for 3 hr. and then filtered hot. The filtrate was evaporated to dryness under reduced pressure and the residue extracted with boiling ethyl acetate (3 × 25 c.c.). Evaporation of the filtered extract afforded 2 : 5-*dihydroxyimino*-3-*methylpyrrolidine* (1·2 g.), m. p. 157—158°, which crystallised from ethyl acetate as prisms, m. p. 161° (Found: C, 41·9; H, 6·1; N, 29·1. $C_5H_9O_2N_3$ requires C, 41·95; H, 6·3; N, 29·4%). It gave a dull violet colour with aqueous ferric chloride and a yellow-green with cupric acetate.

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Department of Chemistry, Imperial College of Science and Technology, London, S.W.7. [*Received, July 22nd*, 1958.]

[14] Fichter and Merckens, *Ber.*, 1901, **34**, 4174.

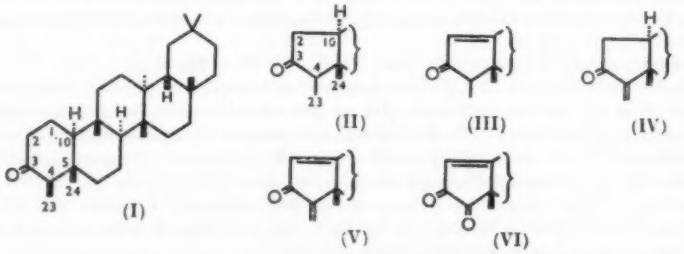
XUM

38. *Triterpenoids. Part LVII.*[1] *The Oxidation of Norfriedelanone with Selenium Dioxide.*

By George Brownlie, F. S. Spring, and Robert Stevenson.

Oxidation of A(1)-norfriedelan-3-one * (II) with selenium dioxide gives A(1)-norfriedel-4(23)-en-3-one (IV). Further oxidation of this αβ-unsaturated ketone with selenium dioxide gives A(1)-norfriedela-2(10) : 4(23)-dien-3-one (V) and A(4)-nor-23-norfriedel-1(10)-ene-2 : 3-dione (VI).

Oxidation of friedelin (I)[2-5] with chromic acid gives friedelindicarboxylic acid, the anhydride of which gives norfriedelanone (II) on pyrolysis.[6] Ruzicka, Jeger, and Ringnes [6] studied the oxidation of norfriedelanone with selenium dioxide and, using acetic acid as solvent, obtained a norfriedelenone of m. p. 260—261°, $[\alpha]_D$ −108°, $\lambda_{max.}$ 2530 Å (log ε 4·2), which was considered to be an αβ-unsaturated ketone. If this diagnosis is correct, possible structures for this compound are (III) and (IV). However, the position of the ultraviolet absorption maximum (2530 Å) is different from that predicted, by using the the usual empirical rules, for either (III) (*ca.* 2340 Å) or (IV) (*ca.* 2300 Å). We have again examined the oxidation of norfriedelanone with selenium dioxide and, using the method described by Ruzicka, Jeger, and Ringnes,[6] we obtained a norfriedelenone having their recorded m. p. and $[\alpha]_D$ but $\lambda_{max.}$ 2290 Å (ε 5500). Its infrared absorption spectrum includes bands at 1642 and 932 cm.$^{-1}$, attributable to a vinylidene group, and the relatively low intensity of its ultraviolet absorption bands is consistent with the presence of a *cisoid* αβ-unsaturated ketone chromophore, so we represent this oxidation product as A(1)-norfriedel-4(23)-en-3-one * (IV). The infrared spectrum of norfriedelanone includes a band at 1738 cm.$^{-1}$, a typical carbonyl stretching frequency for a *cyclo*pentanone. The carbonyl band of A(1)-norfriedel-4(23)-en-3-one (IV) is at 1733 cm.$^{-1}$; the relatively small shift in the carbonyl frequency associated with the conversion of the saturated ketone (II)



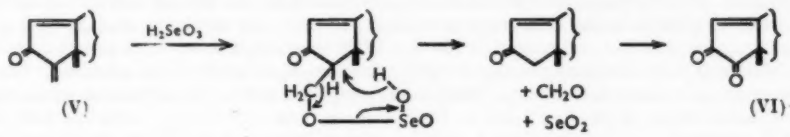
into the αβ-unsaturated ketone (IV) is apparently characteristic of conjugation between a carbonyl group in a five-membered ring and an exocyclic double bond.[7]

Oxidation of norfriedelanone with selenium dioxide in dioxan at 200° gives a product which was originally described as a norfriedelenedione [6] but was subsequently identified [2] as A(4)-nor-23-norfriedel-1(10)-ene-2 : 3-dione (VI). Ruzicka *et al.*[6] also obtained this compound by similar oxidation of their norfriedelenone. We find that A(1)-norfriedel-4(23)-en-3-one (IV) with selenium dioxide in dioxan at 200° gives a mixture

* The friedelin derivatives containing a contracted ring A are named in this paper according to the rules suggested by Allard and Ourisson (*Tetrahedron*, 1957, **1**, 277).

[1] Part LVI, Smith, Smith, and Spring, *Tetrahedron*, 1958, **2**, in the press.
[2] Brownlie, Spring, Stevenson, and Strachan, *J.*, 1956, 2419.
[3] Corey and Ursprung, *J. Amer. Chem. Soc.*, 1956, **78**, 5041.
[4] Takahashi and Ourisson, *Bull. Soc. chim. France*, 1956, 353.
[5] Dutler, Jeger, and Ruzicka, *Helv. Chim. Acta*, 1955, **38**, 1268.
[6] Ruzicka, Jeger, and Ringnes, *ibid.*, 1944, **27**, 972.
[7] Wiesner, Armstrong, Bartlett, and Edwards, *J. Amer. Chem. Soc.*, 1954, **76**, 6068.

separated by chromatography into bisnorfriedelenedione (VI) and a compound, $C_{29}H_{44}O$, m. p. 253—255°, $[\alpha]_D$ +190°, $\lambda_{max.}$ 2520 Å (ε 13,500), which we consider to be A(1)-norfriedela-2(10) : 4(23)-dien-3-one (V). In agreement the infrared spectrum of this diene includes bands at 1706 (>CO of a *cyclo*pentenone), 1650 and 940 (vinylidene), and 1585 and 879 cm.$^{-1}$ (conjugated C:C in the ring). The course of the oxidation of norfriedelanone (II) to bisnorfriedelenedione (VI) with selenium dioxide is now represented as (II) → (IV) → (V) → (VI). This extrusion of a methyl (or methylene) group is, in our experience, unique and a possible mechanism is as annexed.



The difference in the ultraviolet absorption spectrum of our norfriedelenone from that described by Ruzicka *et al.*,[6] coupled with the similar melting points and specific rotations, is curious. It is also remarkable that, although the melting point and ultraviolet absorption spectrum of Ruzicka's norfriedelenone are in fair agreement with those of A(1)-norfriedela-2(10) : 4(23)-dien-3-one (V), the specific rotations of the two compounds are distinct. Although Corey and Ursprung [3] have also described the oxidation of norfriedelanone with selenium dioxide in acetic acid, the ultraviolet absorption spectrum and the specific rotation reported by these authors are apparently quotations of those observed by Ruzicka *et al.*[6] The principal infrared absorption bands observed by them for their preparation of norfriedelenone appear to identify it as A(1)-norfriedela-2(10) : 4(23)-dien-3-one (V).

Experimental

Rotations were measured for $CHCl_3$ and ultraviolet absorption spectra for EtOH solutions. Grade II alumina and light petroleum, b. p. 60—80°, were used for chromatography.

Friedelindicarboxylic Acid.—Friedelin was oxidised with chromium trioxide as described by Ruzicka *et al.*[6] and the acidic oxidation product isolated in the usual way. The acid was esterified by diazomethane, and the neutral ester was chromatographed in light petroleum–benzene (10 : 1). Elution with light petroleum–benzene (1 : 2) gave a fraction which crystallised from chloroform–methanol, yielding dimethyl friedelindicarboxylate as plates, m. p. 175—177°, $[\alpha]_D$ +2·5° (*c* 1·4). Ruzicka *et al.*[6] give m. p. 174—176°, $[\alpha]_D$ +10°. Saponification of the ester with 5% methanolic potassium hydroxide for 3 hr. gave friedelindicarboxylic acid as prisms (from methanol), m. p. 287—288°. Ruzicka *et al.*[6] give m. p. 288°, $[\alpha]_D$ +21°.

Friedelindicarboxylic anhydride was prepared from the dicarboxylic acid as described by Ruzicka *et al.*[6] It separates from acetic anhydride as needles, m. p. 264—266°, $[\alpha]_D$ +75·5° (*c* 0·9). Ruzicka *et al.*[6] give m. p. 264—265°, $[\alpha]_D$ +74°.

A(1)-*Norfriedelan*-3-*one*.—Friedelindicarboxylic anhydride (1 g.) was heated at 280° for 1 min. The pressure was then reduced to 14 mm. and heating continued. The combined residue and sublimate were dissolved in light petroleum and chromatographed on alumina. Elution with benzene and crystallisation of the product from chloroform–methanol gave norfriedelanone (600 mg.) as plates, m. p. 232—235°, $[\alpha]_D$ −84° (*c* 1·2), $\nu_{max.}$ (in Nujol) 1730 cm.$^{-1}$ (Found: C, 84·1; H, 11·85. Calc. for $C_{29}H_{48}O$: C, 84·4; H, 11·7%). Ruzicka *et al.*[6] give m. p. 231—232°, $[\alpha]_D$ −84°.

A(1)-*Norfriedel*-4(23)-*en*-3-*one*.—A solution of norfriedelanone (100 mg.) in acetic acid (10 c.c.) was refluxed with selenium dioxide (220 mg.) for 30 min. The solution was filtered and the yellow filtrate worked up in the usual way. Crystallisation of the product (70 mg.) from chloroform–methanol gave blades, m. p. 259—261°, $[\alpha]_D$ −97° (*c* 1·2). Purification of this product by chromatography to remove a slight yellow colour, and crystallisation from chloroform–methanol, gave A(1)-*norfriedel*-4(23)-*en*-3-*one* as blades, m. p. 261—263°, $[\alpha]_D$ −104° (*c* 1·1), $\lambda_{max.}$ 2290 Å (ε 5500), $\nu_{max.}$ (in CS_2) 1733 s, 1642 w, 932 m cm.$^{-1}$ (Found: C, 84·85;

H, 11·6. $C_{29}H_{46}O$ requires C, 84·8; H, 11·3%). It does not give a colour with tetranitromethane. Repetition of the experiment under the exact conditions described by Ruzicka *et al.*[6] gave the same product.

A(1)-*Norfriedel*-4(23)-*en*-3-*ol*.—Lithium aluminium hydride (50 mg.) was added to a solution of A(1)-norfriedel-4(23)-en-3-one (50 mg.) in ether (20 c.c.), and the mixture kept overnight. The product was isolated without the use of mineral acid and crystallised from chloroform–methanol to give A(1)-*norfriedel*-4(23)-*en*-3-*ol* as small plates, m. p. 250—253°, $[\alpha]_D$ +41° (*c* 0·5), ε_{2940} 1150 (Found: C, 84·0; H, 11·4. $C_{29}H_{46}O$ requires C, 84·4; H, 11·7%). The alcohol does not give a colour with tetranitromethane.

Oxidation of A(1)-*Norfriedel*-4(23)-*en*-3-*one with Selenium Dioxide at* 200°.—Solutions of A(1)-norfriedel-4(23)-en-3-one (280 mg.) in dioxan (12 c.c.) and selenium dioxide (1·0 g.) in dioxan (3 c.c.) were mixed and heated at 200° for 16 hr. in a sealed tube. The product, isolated in the usual way, was chromatographed in light petroleum–benzene (2 : 1) on alumina. Elution with benzene gave a fraction (50 mg.) which on crystallisation from chloroform–methanol gave A(1)-*norfriedela*-2(10) : 4(23)-*dien*-3-*one* as blades, m. p. 253—255°, $[\alpha]_D$ +190° (*c* 0·8), $\lambda_{max.}$ 2520 Å (ε 13,500), $\nu_{max.}$ (in CCl_4) 1704 s, 1650 w, 1585 m, 940 m, 879 m cm.$^{-1}$ (Found: C, 85·5; H, 11·2. $C_{29}H_{44}O$ requires C, 85·2; H, 10·9%). A mixture with A(1)-norfriedel-4(23)-en-3-one had m. p. 241—244°. Continued elution of the column with benzene–ether (1 : 1) gave a fraction (30 mg.) which on crystallisation from methanol gave A(4)-nor-23-norfriedel-1(10)-ene-2 : 3-dione as orange needles, m. p. 266—268°, $[\alpha]_D$ +235° (*c* 2·0), $\lambda_{max.}$ 2800 Å (ε 7500), $\nu_{max.}$ (in $CHCl_3$) 1764 m, 1712 s, 1575 m, 874 w cm.$^{-1}$. Ruzicka *et al.*[6] give m. p. 269—270° $[\alpha]_D$ +241°, $\lambda_{max.}$ 2800 Å (ε 10,000).

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39. *Solvent Extraction Studies. Part III. The Extraction of Hydrogen Peroxide into Tri-n-butyl Phosphate.*

By D. G. TUCK.

The extraction behaviour of hydrogen peroxide (up to 6·5M-H_2O_2 in the equilibrium aqueous phase) into tri-*n*-butyl phosphate can be explained in terms of the replacement of water in the organic phase by hydrogen peroxide. The effect of the addition of an inert solvent to the organic phase has been studied. For dilute hydrogen peroxide the temperature coefficient of the extraction leads to $\Delta H = -2{\cdot}1$ kcal./mole.

HYDROGEN peroxide is extractable into basic organic solvents such as diethyl ether,[1,2,3] ethyl acetate,[3,4] *iso*butanol,[3] and pentyl alcohol.[5-9] Paulsen[10] recently gave qualitative results on the extraction into a wide range of compounds. I have used tri-*n*-butyl phosphate because it solvates many inorganic compounds[11] and water is very soluble in it.[12,13,14]

EXPERIMENTAL

Materials.—Both Analytical Reagent and laboratory grade hydrogen peroxide were used; no difference in extractive behaviour was observed. Solutions were analysed by titration with potassium permanganate solution.

[1] Kolosovskii, *Bull. Soc. chim. France*, 1925, **37**, 372.
[2] Maass and Hatcher, *J. Amer. Chem. Soc.*, 1916, **38**, 633.
[3] Walton and Lewis, *ibid.*, 1922, **44**, 2472.
[4] Kolosovskii and Kulikov, *Ukrain. khim. Zhur.*, 1934, **9**, 37.
[5] Calvert, *Z. phys. Chem.*, 1901, **38**, 513.
[6] Joyner, *Z. anorg. Chem.*, 1912, **77**, 103.
[7] Menzel, *Z. phys. Chem.*, 1923, **105**, 402.
[8] Husain, *Z. anorg. Chem.*, 1928, **177**, 215.
[9] Livingston, *J. Amer. Chem. Soc.*, 1928, **50**, 3204.
[10] Paulsen, *Chem. and Ind.*, 1956, 1274.
[11] See, for example, Healy and McKay, *Rec. Trav. chim.*, 1956, **75**, 730.
[12] Moore, U.S.A.E.C. report AECD–3196.
[13] Alcock, Grimley, Healy, Kennedy, and McKay, *Trans. Faraday Soc.*, 1956, **52**, 39.
[14] Tuck, *J.*, 1958, 2783.

Tri-*n*-butyl phosphate was purified as described previously [14] and stored over chromatographic alumina to prevent peroxide formation.[15] In certain experiments, the solvent was diluted with " AnalaR " carbon tetrachloride.

Procedure.—5 ml. of hydrogen peroxide solution and 5 ml. of tri-*n*-butyl phosphate were shaken in a stoppered bottle for 20 min., then centrifuged. Suitable aliquot parts were analysed. Samples of the organic phase were dissolved in *ca.* 25 ml. of aqueous acetone before titration; it was shown that direct measurement of the amount of extracted hydrogen peroxide was thus possible. Hydrogen peroxide did not decompose in any solution for which results are reported.

In investigating the effect of temperature, both phases were allowed to reach the temperature of the thermostat before mixing; after equilibration, aliquot portions were weighed and analysed, and extraction coefficients calculated on a molal basis. All other experiments were carried out at room temperature (23°).

The increase in the volume of the organic phase [16] was not significantly different from that observed on saturation with water.[14] A value of 5·35 ml. was taken for the volume of the equilibrium organic phase.

Determination of Water in Tri-n-*butyl Phosphate.*—The Karl Fischer volumetric determination of water is unaffected by hydrogen peroxide,[17,18] but I found that if more is present than the sulphur dioxide in the reagent (Fischer Scientific Co.) can take up its reaction with iodine gives high results for the water concentration. Anhydrous sulphur dioxide was therefore passed through silica gel to remove traces of water vapour, and bubbled through an aliquot portion of the organic phase in the previously dried titration vessel, from which atmospheric moisture was excluded; results were then reproducible. A dead-stop end-point method was used; the Karl Fischer reagent was calibrated with " AnalaR " sodium tartrate.

Results and Discussion

Extraction into Pure Tri-n-*butyl Phosphate.*—Table 1 gives the results (org. = organic phase; aq. = aqueous phase). The gradual decrease in the extraction coefficient, also

Table 1. *Extraction of hydrogen peroxide into tri*-n-*butyl phosphate.*

H_2O_2 (M), aq.	0·605	0·835	1·46	2·53	3·44	4·22	4·44	5·43	6·41
H_2O_2 (M), org.....	0·32	0·408	0·639	0·944	1·13	1·32	1·38	1·54	1·76
$E_{H_2O_2}$	0·525	0·49	0·44	0·37	0·33	0·31	0·31	0·28	0·275

found by Kolosovskii [1] and by Paulsen [10] for other solvents, is due to a decrease in the concentration of available solvent with increasing amounts of hydrogen peroxide in the organic phase. The constant value of $E_{H_2O_2}$ for the extraction into pentyl alcohol [5,6,7,8,9] at different hydrogen peroxide concentrations is presumably due to the hydroxylic nature of this solvent.

Since tri-*n*-butyl phosphate extracts water,[12,13,14] it seems likely that extraction of hydrogen peroxide displaces water from the organic phase. This is confirmed by the results of Karl Fischer titrations (Table 2). Within experimental limits, the sum of water

Table 2. *Water content of tri*-n-*butyl phosphate solutions of hydrogen peroxide.*

H_2O (M)	3·45	3·02	2·74	2·70	2·35	2·13	2·18
H_2O_2 (M)	0	0·37	0·70	0·86	1·16	1·28	1·48
Total	3·45	3·39	3·44	3·56	3·51	3·41	3·66

and hydrogen peroxide concentrations is constant at an average of 3·49 $\pm$ 0·08 mmoles/ml. The figure for water-saturated tri-*n*-butyl phosphate, 3·45 $\pm$ 0·70M, is the mean of three determinations and three calibrations. Pure tri-*n*-butyl phosphate is 3·65M, but on allowing for the volume increase due to saturation,[14] this value is reduced to 3·43M, equal to the water concentration within experimental error.

[15] Dasler and Bauer, *Ind. Eng. Chem. Anal.*, 1946, **18**, 52.
[16] Tuck, *J.*, 1957, 3202.
[17] Zimmerman, Felte, and Seifer, *Fette u. Seifen*, 1939, **46**, 446.
[18] Mitchell and Smith, " Aquametry," Interscience Publishers, Inc., New York, 1948, p. 253.

Treating the system as a competition between water and hydrogen peroxide for the organic solvent, one can write

$$\frac{K_1}{K_2} = \frac{[Bu_3PO_4,H_2O][H_2O_2(aq)]}{[Bu_3PO_4,H_2O_2][H_2O(aq)]} \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where K_1 and K_2 are the respective mass-action constants for the formation of Bu_3PO_4,H_2O and Bu_3PO_4,H_2O_2. Over the concentration range studied, one can neglect the aqueous phase activity coefficients of both water and hydrogen peroxide. It will also be assumed that the activities of the species in the organic phase can be equated with the concentrations; eqn. (1) then becomes

$$K' = \frac{(\text{mole ratio } H_2O/H_2O_2, \text{ organic phase})}{(\text{mole ratio } H_2O/H_2O_2, \text{ aqueous phase})}$$

Table 3 shows that K' is reasonably constant, justifying the assumptions.

TABLE 3. *Mole ratios, water : hydrogen peroxide, in organic and aqueous phases.*

H_2O_2 (M), org. ...	0·32	0·41	0·64	0·94	1·13	1·38	1·54	1·76
H_2O (M),* org. ...	3·11	3·02	2·79	2·49	2·30	2·05	1·89	1·67
$H_2O : H_2O_2$, org....	9·74	7·40	4·37	2·64	2·04	1·49	1·23	0·95
$H_2O : H_2O_2$, aq. ...	91·5	66·2	38·3	21·7	15·8	12·2	9·94	8·38
K'	0·106	0·112	0·114	0·122	0·129	0·122	0·124	0·113

* By difference.

The mean value of $K' = 0·118 \pm 0·004$ shows that K_2 is about $8·5K_1$, presumably because the stronger acidity of hydrogen peroxide ($pK = 11·75$ [19]) causes stronger complexing with the basic solvent.

Effect of Inert Solvent.—Aqueous hydrogen peroxide (3% v/v) was extracted into mixtures of tributyl phosphate and carbon tetrachloride (Table 4). Hydrogen peroxide

TABLE. 4. *Extraction of hydrogen peroxide into* Bu_3PO_4–CCl_4 *mixtures.*

Bu_3PO_4 (% v/v)	100	80	60	40	20
H_2O_2 (M), aq.	0·95	1·06	1·17	1·28	1·33
H_2O_2 (M), org.	0·45	0·33	0·21	0·10	0·029
$E_{H_2O_2}$	0·47	0·31	0·18	0·079	0·022

was almost completely insoluble in carbon tetrachloride (as in benzene [2]). Comparison with the results of McKay and his co-workers [13] suggests that the extraction of hydrogen peroxide falls off more slowly than does the uptake of water with decreasing tributyl phosphate concentration. This is again presumably due to the more acidic character of hydrogen peroxide; the interaction of tri-*n*-butyl phosphate with nitric acid is virtually unaffected by non-polar solvents.[13,14]

Effect of Temperature.—In measuring the effect of temperature on the extraction, the constant

$$K_T = \frac{\text{mole ratio, organic phase}}{\text{aq. } H_2O_2 \text{ concn. (molal)}}$$

was evaluated (Table 5). A decrease in $E_{H_2O_2}$ for ether with increasing temperature was reported by Walton and Lewis [3] and by Paulsen.[10] The present results give a linear plot

TABLE. 5. *Effect of temperature change on the extraction of hydrogen peroxide into tri-*n*-butyl phosphate.*

Temp.	H_2O_2 (m), aq.	$E_{H_2O_2}$	Mole ratio, org.	K_T
15·1°	0·590	0·570	0·107	0·182
24·9	0·609	0·516	0·100	0·164
35·2	0·649	0·452	0·094	0·144

[19] Evans and Uri, *Trans. Faraday Soc.*, 1949, **45**, 224.

of log K_T against $1/T°$ K; the slope corresponds to $\Delta H = -2{\cdot}1$ kcal./mole. Similar values have been found for systems involving the extraction of chloroferric acid [20] and of molybdenum(VI) compounds.[21]

It is noteworthy that a solution of hydrogen peroxide in tri-*n*-butyl phosphate has many of the redox properties of the corresponding aqueous solution (cf. Walton and Jones [22]), and that reaction with an extract solution of chromium(VI) in this solvent [23] produces the well-known blue colour of perchromic acid; it is hoped to investigate this reaction later.

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[20] Nachtrieb and Conway, *J. Amer. Chem. Soc.*, 1948, **70**, 3547.
[21] Diamond, personal communication.
[22] Walton and Jones, *J. Amer. Chem. Soc.*, 1916, **38**, 1956.
[23] Diamond and Tuck, unpublished results.

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40. *Aspects of Stereochemistry. Part XI.* Epoxide Formation in the* cyclo*Hexene and* bicyclo*Heptene Series.*

By H. B. HENBEST and B. NICHOLLS.

On reaction with *cyclo*hexenes with $CH_2{\cdot}OH$, $CH_2{\cdot}OAc$, or CO_2Me substituents at the 4-position, approach of perbenzoic acid is preferentially *trans* to the substituent. In the *bicyclo*heptene series the usual direction of attack of peracids (on the same side as the methylene bridge) is not altered by substituents (OH, OAc, $CH_2{\cdot}OAc$, CO_2H, or CO_2Me) on the other side of the ring. However, in the case of a hydroxymethyl substituent the isolation of a tetrahydrofuran derivative and a high reaction velocity indicate that the primary alcohol group is rendering intramolecular nucleophilic assistance to the olefin–peracid reaction. The epoxide from "*endo*-dehydronorborneol" is isomerized by alkali to an oxetan derivative, the reaction confirming the accepted configuration of the initial olefinic alcohol.

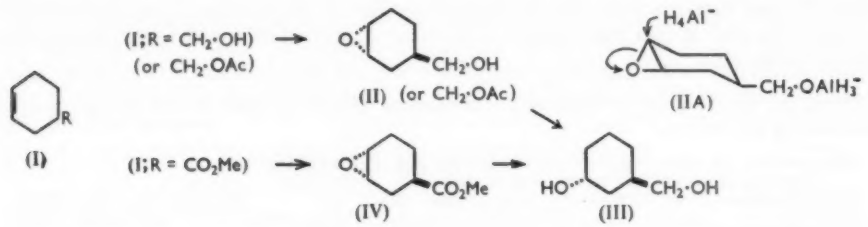
PREVIOUS studies have shown that some positive directing effect is involved in the reaction of *cyclo*hex-2-enol with peracids, as a *cis*-hydroxy-epoxide is obtained as the major product.[1,2] In contrast, *cyclo*hex-3-enol gave a mixture of the *cis*- and *trans*-isomers.[2] This work has now been extended to some compounds related to *cyclo*hex-3-enol in which the hydroxyl group has been replaced by bulkier groups, as in (I; R = $CH_2{\cdot}OH$, $CH_2{\cdot}OAc$, or CO_2Me). Each of these *cyclo*alkenes gave a liquid epoxide, homogeneous on distillation and reduced by lithium aluminium hydride to the known [3] *trans*-diol (III). The formation of this 1 : 3-compound by hydride reduction may be visualized as proceeding from conformations (IIA) (bulky aluminohydride complex equatorial), opening of the epoxide ring giving the axial 3-alcohol. The lower homologue of the epoxy-alcohol (II; $CH_2{\cdot}OH$), with hydroxyl in place of the hydroxymethyl group, gave the 1 : 4-product on hydride reduction by an intramolecular mechanism involving a six-ring transition state.[2] The similar reduction of the higher homologue (II; $CH_2{\cdot}OH$) would involve an unlikely seven-ring transition state, and the more usual reaction (cf. IIA) therefore takes place.

Recent work [4] has shown that the *trans*-isomer is the major product from the reaction

* Part X, *J.*, 1958, 3293.

[1] Henbest and Wilson, *J.*, 1957, 1958.
[2] Henbest and Nicholls, *J.*, 1957, 4608.
[3] Clarke and Owen, *J.*, 1950, 2108.
[4] Hopff and Hoffmann, *Helv. Chim. Acta*, 1957, **40**, 1585.

of 4-phenyl*cyclo*hexene (I; R = Ph) with peracetic acid. On the other hand our own preliminary observations have shown that a mixture of epoxides results from the reaction of the nitrile (I; R = CN) with perbenzoic acid. So far, the results in the *cyclo*hexene series seem to suggest that *trans*-isomers tend to be formed when the 4-substituent is



relatively bulky (CH_2·OH, CH_2·OAc, CO_2Me, Ph), whereas mixtures are produced from *cyclo*alkenes with smaller 4-substituents (OH, CN). If further work should establish that *trans*-approach is caused by steric factors, the effectiveness of the moderately remote groups at the 4-position is noteworthy since in the preferred conformation the substituent lies approximately in the plane of the ring in an equatorial or slightly distorted equatorial position.

bicyclo*Heptene Series.—Nomenclature.* The convenient αβ-prefix system has been used [5] in bicyclic compounds to denote the configurations of substituents relative to a bridge. In continuity with this usage and with our own usage of these prefixes in other alicyclic compounds,[6] the configurations of substituents in the *bicyclo*heptane series will be denoted by α and β (the latter signifying a group *cis* to the methylene bridge) instead of the *endo*- and *exo*-terms. The latter terms have recently been used in a somewhat different sense to denote the direction of reagent approach towards trigonal carbon in the *cyclo*hexane series.[7,8]

Results. The first compound studied in the bicyclic series was the unsaturated alcohol (V), which may be regarded as a methylene-bridged analogue of the *cyclo*hex-3-enol that was investigated earlier. In the *bicyclo*heptene series, reagents normally approach the double bond on the less hindered β-side, and the reaction of the olefinic alcohol (V) was no exception to this rule, isolation of the crystalline *trans*-hydroxy-epoxide (VI) in high yield showing that the hydroxyl group was exerting no detectable directing effect of the kind observed with cyclic allylic alcohols.[1]

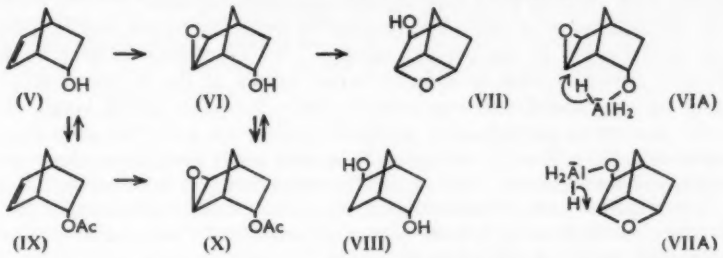
The *trans*-configuration of the new epoxide (VI) was established by the following reactions. Treatment with potassium *tert.*-butoxide in *tert.*-butyl alcohol gave an isomeric hydroxy-epoxide (VII) that exhibited a strong infrared band at 940 $cm.^{-1}$, analogous to that given at 950 $cm.^{-1}$ by 2 : 2-dimethyloxetane. [All the *vic.*-epoxides of the *bicyclo*heptane series (*e.g.*, VI and X) gave a strong band near 850 $cm.^{-1}$ (cf. ref. 9).] Both epoxides (VI and VII) were reduced by lithium aluminium hydride to the same diol, formulated as (VIII). The unidirectional opening of the epoxide ring in each case may be due to the *trans*-disposition of the groups which would cause the reactions to proceed *via* cyclic transition states (VIA and VIIA) similar to those proposed for the monocyclic series.[1,2] Acetylation of the initial hydroxy-epoxide (VI) gave the epoxy-acetate (X), also obtained directly in high yield from the unsaturated acetate (IX) and perbenzoic acid.

It may be noted that these reactions, particularly the isomerization, (VI ⟶ VII),

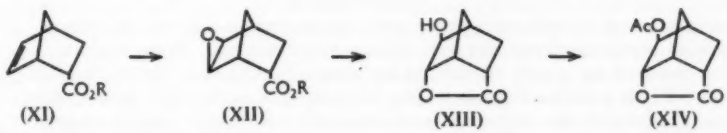
[5] *Inter alia*, Fodor and Nádor, *J.*, 1953, 721; Cookson, *J.*, 1954, 282.
[6] Henbest, Smith, and Thomas, *J.*, 1958, 3293; see also following paper.
[7] Zimmerman, *J. Amer. Chem. Soc.*, 1956, **78**, 1168.
[8] Bordwell and Hewett, *ibid.*, 1957, **79**, 3493.
[9] Meinwald, Nozaki, and Wiley, *ibid.*, p. 5580.

XUM

provide rather direct proof for the accepted α-configuration of the unsaturated alcohol (V) and the acetate (IX; a Diels–Alder adduct) from which it is prepared.[10]

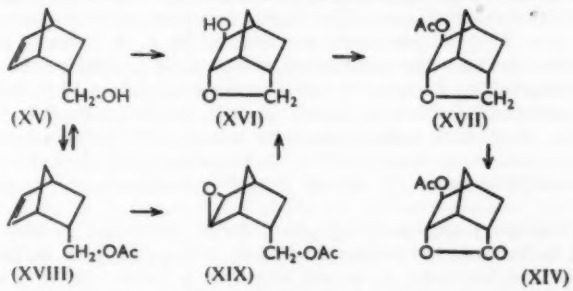


The reaction of perbenzoic acid with the unsaturated ester (XI; R = Me) (equivalent to I; R = CO_2Me with an extra methylene bridge) gave a homogeneous product formulated as the β-epoxide (XII; R = Me). On treatment with aqueous formic acid this epoxide yielded the hydroxy-lactone (XIII) (carbonyl band at 1750 cm.$^{-1}$), also isolated when the



unsaturated ester (XI; R = Me) was treated with a formic acid–hydrogen peroxide mixture. The acetate (XIV) was obtained on acetylation and also by another route (below). The infrared absorption of the crude product from the reaction of perbenzoic acid with the unsaturated acid (XI; R = H) indicated that the epoxy-acid (XII; R = H) had been formed, but attempts to separate it from benzoic acid by crystallization were frustrated by its ready isomerization to the hydroxy-lactone (XIII).

Reactions of the unsaturated alcohol (XV) (structurally related to I; R = CH_2·OH) and some of its derivatives with peracid have also been examined. The methyl ether of (XV) and the acetate (XVIII) reacted with perbenzoic acid at normal rates and in a preparative experiment the acetate gave a good yield of an epoxide which had a strong absorption band at 850 cm.$^{-1}$ and may therefore be formulated as the β-epoxide (XIX).



However, the parent alcohol (XV) reacted with the peracid at an abnormally rapid rate to give a product formulated as (XVI). This structure is suggested because the compound (*a*) was recovered unchanged after treatment with lithium aluminium hydride and (*b*) gave a crystalline acetate (XVII) different from the previously obtained epoxy-acetate (XIX), and (*c*), because the alcohol and its acetate each exhibited a strong ether band near 1150 cm.$^{-1}$, also shown by the corresponding compound lacking the hydroxyl (or acetoxyl)

[10] Alder and his co-workers, *Annalen*, 1936, **525**, 183, 201; 1939, **543** 1.

group (following paper). The ease of formation of the tetrahydrofuran ring structure was also shown by the formation of the hydroxy-ether (XVI) from the epoxy-acetate (XIX) on treatment with alkali or even with lithium aluminium hydride.

Clearly the proximity of the α-hydroxymethyl grouping to the double bond in (XV) causes its participation in the peracid reaction; in the related monocyclic alcohol (I; R = CH_2·OH) normal vicinal epoxide formation occurs as the hydroxymethyl group is presumably equatorial and well separated in space from the double bond. In bicyclic compounds, analogous participation probably takes place in the conversion of the α-carboxylic acid (XI; R = H) into an iodo-lactone under conditions where the isomeric β-carboxylic acid is unaffected,[11] and also in the mercuration of the alcohol (XV) (following paper). For reactions with perbenzoic acid, the present results indicate that participation by an α-hydroxymethyl group is more powerful than that by an α-carboxylic acid group, in line with their relative nucleophilic strengths.

As the position adjacent to an ether group is often susceptible to oxidation, the preparation of the acetoxy-lactone (XIV) from the acetoxy-ether (XVII) was thought possible. This conversion was effected in good yield by use of chromic acid in acetone.

Experimental

M. p.s in this and the following paper were determined on a Kofler hot stage. The peracid reactions were performed at 0° and were followed by titration. When reaction was complete, acids were removed by means of calcium hydroxide.[3] Alumina was deactivated with dilute acetic acid. Light petroleum refers to the fraction of b. p. 60—80° unless otherwise stated. The infrared spectra of all compounds were consistent with the structures assigned. As stated on p. 222 the αβ-system of nomenclature is used for denoting relative configuration in racemic compounds.[6] As none of these was resolved, the (±)-prefix has been omitted throughout the two papers.

Reactions of cyclo*Hex*-3-*enylmethanol* (I; R = CH_2·OH) *and its Acetate with Perbenzoic Acid.*—The reaction mixture from the unsaturated alcohol (5·55 g.) and perbenzoic acid in ether (100 c.c.; 0·64M) was shaken with calcium hydroxide (25 g.) until neutral. Isolation in the usual way gave 3α : 4α-*epoxy*-1β-cyclo*hexylmethanol* (II) (5·93 g., 90%), b. p. 64°/0·3 mm., n_D^{21} 1·4828 (identical for six fractions) (Found: C, 65·5; H, 9·3. $C_7H_{12}O_2$ requires C, 65·6; H, 9·4%). The α-*naphthylurethane*, formed in high yield, separated from light petroleum (b. p. 80—100°) as needles, m. p. 112—114° (Found: C, 72·9; H, 6·3. $C_{18}H_{19}O_3N$ requires C, 72·7; H, 6·4%).

The epoxy-alcohol (2·8 g.) was reduced with lithium aluminium hydride (1·01 g.) in ether (70 c.c.) in the usual way.[3] Distillation gave 3α-hydroxy-1β-*cyclo*hexylmethanol (III) (2·66 g.), b. p. (bath-temp.) 122—125°/0·03 mm. The bisphenylurethane, formed in good yield, had m. p. and mixed m. p. 118—120° (sample kindly provided by Dr. L. N. Owen of Imperial College).

A similar reaction between the unsaturated acetate (7·74 g.) and perbenzoic acid in ether (100 c.c.; 0·64M) afforded 3α : 4α-*epoxy*-1β-cyclo*hexylmethyl acetate* (8·12 g., 95%), b. p. 57°/0·25 mm., n_D^{21} 1·4625 (identical for five fractions) (Found: C, 63·5; H, 8·3. $C_9H_{14}O_3$ requires C, 63·5; H, 8·3%). Hydrolysis of the epoxy-ester (2·46 g.) with potassium hydroxide (1·04 g.) in methanol (30 c.c.) and water (2 c.c.) yielded the foregoing epoxy-alcohol (1·73 g., 90%), b. p. (bath-temp.) 85—94°/0·05 mm., n_D^{20} 1·4840 (α-naphthylurethane, m. p. and mixed m. p. 112—114°).

Reduction of the epoxy-acetate (3·7 g.) with lithium aluminium hydride (1·7 g.) in ether (100 c.c.) yielded 3α-hydroxy-1β-*cyclo*hexylmethanol (2·49 g., 88%), b. p. (bath-temp.) 120—125°/0·04 mm. (bisphenylurethane, m. p. and mixed m. p. 117·5—120°).

Reaction of Methyl cyclo*Hex*-3-*ene*-1-*carboxylate with Perbenzoic Acid.*—The reaction between the unsaturated ester (7·07 g.) and perbenzoic acid in ether (93 c.c., 0·65M) gave *methyl* 3α : 4α-*epoxy*cyclo*hexane*-1β-*carboxylate* (IV) (7·49 g., 95%), b. p. 50—51°/0·5 mm., n_D^{21} 1·4630 (six fractions) (Found: C, 61·35; H, 7·75. $C_8H_{12}O_3$ requires C, 61·5; H, 7·75%).

The epoxy-ester (3·43 g.) was reduced with lithium aluminium hydride (2 g.) in ether (100 c.c.) in the usual way to 3α-*hydroxy*-1β-cyclo*hexylmethanol* (III) (2·8 g.), b. p. (bath-temp.) 125—130°/0·05 mm. (bisphenylurethane, m. p. and mixed m. p. 118—120°).

[11] Rondestvedt and Ver Nooy, *J. Amer. Chem. Soc.*, 1955, **77**, 4878.

Reactions of bicyclo[2 : 2 : 1]*Hept-5-en-2α-ol* (V) *and its Acetate* (XI) *with Perbenzoic Acid.*—The reaction mixture from the alcohol (3·76 g.) and perbenzoic acid in ether (100 c.c. of a 0·43M-solution) was shaken with calcium hydroxide (20 g.) until neutral. One crystallization of the product from ether–pentane gave material (4·01 g., 93%), m. p. 155—161° (sublimes). The pure 5β : 6β-*epoxy*bicyclo[2 : 2 : 1]*heptan-2α-ol* (VI) had m. p. 160—162° (sublimes) (Found: C, 66·7; H, 7·9. $C_7H_{10}O_2$ requires C, 66·65; H, 8·0%). Its *α-naphthylurethane* had m. p. 143·5—145° (from light petroleum) (Found: C, 72·9; H, 6·0. $C_{18}H_{17}O_2N$ requires C, 73·2; H, 5·8%). Acetylation gave the *epoxy-acetate* (X), b. p. 114—115°/14 mm., m. p. 52·5—54° (from pentane) (Found: C, 64·55; H, 7·05. $C_9H_{12}O_3$ requires C, 64·3; H, 7·1%).

The reaction mixture from the unsaturated acetate (10 g.) and perbenzoic acid in ether (125 c.c. of a 0·59M-solution) was shaken with calcium hydroxide (28 g.) until neutral. Distillation gave the epoxy-acetate which solidified. Crystallization from pentane gave the epoxy-acetate (9·75 g., 88%), m. p. and mixed m. p. with the foregoing compound, 53—54°. For hydrolysis, the epoxy-acetate (3·76 g.) and potassium hydroxide (1·2 g.) in methanol (40 c.c.) and water (5 c.c.) were kept at 20° for 24 hr. Isolation with ether gave the epoxy-alcohol (2·66 g.), m. p. and mixed m. p. 159—162° (sublimes) (α-naphthylurethane, m. p. and mixed m. p. 143—145°).

Reduction of the Epoxy-alcohol (VI).—The epoxy-alcohol (2·46 g.) was added to lithium aluminium hydride in ether (50 c.c.; 0·4M) and heated under reflux for 3 hr. Decomposition with ethyl acetate and dilute acid, followed by continuous extraction with ether, gave a solid (2·49 g.), m. p. 162—210°. Crystallization from benzene gave a sparingly soluble compound (0·24 g.), m. p. 223—227°, probably a triol. The remainder was chromatographed on deactivated alumina (200 g.). Elution with benzene–ether (1 : 1) gave starting material (0·18 g.). Elution with ether gave bicyclo[2 : 2 : 1]*heptane*-2β : 5α-*diol* (VIII) (1·77 g.), m. p. 191—192·5° (from benzene–*iso*propyl ether) (Found: C, 65·5; H, 9·3. $C_9H_{12}O_2$ requires C, 65·6; H, 9·4%). Its *di*-p-*bromobenzenesulphonate* had m. p. 151·5—154° (from ethyl acetate–*iso*propyl ether) (Found: C, 40·0; H, 3·5. $C_{19}H_{18}O_6Br_2S_2$ requires C, 40·6; H, 3·25%).

Isomerization of the Epoxy-alcohol (VI).—Solutions of the epoxy-alcohol (3·02 g.) in *tert.*-butyl alcohol (75 c.c.) and potassium *tert.*-butoxide in *tert.*-butyl alcohol (10 c.c.; M) were mixed and kept at 20° for 4 days, previous small-scale experiments having shown that this time was necessary for complete isomerization (disappearance of *vic.*-epoxide band at 850 cm.$^{-1}$). The solution was filtered through deactivated alumina (100 g.), and the solvent removed through a Fenske column. Recrystallization from ethyl acetate–light petroleum followed by sublimation gave 3α : 5α-*epoxy*bicyclo[2 : 2 : 1]*heptan-2β-ol* (VII) (2·47 g., 82%), m. p. 173—176° (Found: C, 66·7; H, 8·1. $C_7H_{10}O_2$ requires C, 66·65; H, 8·0%).

The 3α : 5α-epoxide (0·816 g.) and lithium aluminium hydride (0·4 g.) in dry dioxan (10 c.c.) were heated under reflux for 36 hr. After decomposition of the excess of hydride, the diol was isolated by continuous ether-extraction. Recrystallization from ether acetate–*iso*propyl ether and sublimation in a short-path still at 130°/0·2 mm. gave *bicyclo*[2 : 2 : 1]heptane-2β : 5α-diol (VIII) (0·753 g., 90%), m. p. and mixed m. p. 192—194°.

Reactions of bicyclo[2 : 2 : 1]*Hept-5-en-2α-ylmethanol* (XV) *and its Acetate* (XVIII) *with Perbenzoic Acid.*—The reaction mixture from the alcohol (10·02 g.) in ether (50 c.c.) and perbenzoic acid in ether (161 c.c.; 0·59M) was shaken with calcium hydroxide (40 g.). Distillation at 110° (bath-temp.)/0·1 mm. gave the crude product (10·83 g.) as a hygroscopic solid, m. p. 115—130°. The pure 6-*oxa*tricyclo[3 : 2 : 1 : $1^{3:8}$]*nonan*-4β-*ol* (XVI) had m. p. 147—150° (from benzene–light petroleum) (Found: C, 68·3; H, 8·6. $C_8H_{12}O_2$ requires C, 68·55; H, 8·65%). Acetylation with acetic anhydride and pyridine at 20° yielded the *acetate* (XVII), m. p. 50—52° (from pentane) (Found: C, 66·0; H, 7·9. $C_{10}H_{14}O_3$ requires C, 65·9; H, 7·75%). The hydroxy-ether (XVI) was unchanged after treatment with lithium aluminium hydride in boiling ether for 3 hr.

The reaction mixture from the unsaturated acetate (XVIII) (10·01 g.) and perbenzoic acid in ether (120 c.c.; 0·58M) was shaken with calcium hydroxide (40 g.). Distillation yielded 5β : 6β-*epoxy*bicyclo*hept*[2 : 2 : 1]-2α-*ylmethyl acetate* (XIX) (10·59 g., 95%), b. p. 129—130°/12 mm., n_D^{23} 1·4813 (constant for 5 fractions) (Found: C, 65·8; H, 7·35. $C_{10}H_{14}O_3$ requires C, 65·9; H, 7·75%). Part of the epoxy-acetate (4·01 g.) was treated with potassium hydroxide (1·51 g.) in methanol (45 c.c.) and water (5 c.c.). Isolation with ether gave a wax (3·04 g.), m. p. 111—127°, which on sublimation (120°/0·2 mm.) and crystallization from benzene–light petroleum gave the hydroxy-ether (XVI) identified as its acetate, m. p. and mixed m. p.

50—52°. This hydroxy-ether was also obtained on treating the *vic.*-epoxy-ester (3·58 g.) with lithium aluminium hydride (2 g.) in ether (200 c.c.).

The starting *acetate* (XVIII) was prepared from the alcohol (XV) in the usual way; it had b. p. 89·5—90°/13 mm., n_D^{15} 1·4733 (Found: C, 70·85; H, 8·45. $C_{10}H_{14}O_2$ requires C, 71·1; H, 8·4%).

Reaction of Methyl bicyclo[2 : 2 : 1]*Hept-5-ene-2α-carboxylate* (XI; R = Me) *with Perbenzoic Acid.*—The reaction solution from the ester (15 g.) and perbenzoic acid in ether (250 c.c.; 0·43M) was neutralized with calcium hydroxide (70 g.). Distillation gave *methyl* 5β : 6β-*epoxy*bicyclo[2 : 2 : 1]*heptane-2α-carboxylate* (XII; R = Me) (16·45 g., 98%), b. p. 122·5—124°/17 mm., n_D^{23} 1·4812 (constant for 5 fractions) (Found: C, 64·5; H, 7·0. $C_9H_{12}O_3$ requires C, 64·25; H, 7·2%).

Formation of the Acetoxy-lactone (XIV).—(*a*) The unsaturated acid (XI; R = H) (2·51 g.) [or its methyl ester (2·73 g.)] was dissolved in 98% formic acid (5·8 g.) at 45° and hydrogen peroxide (2·3 g.; 100-vol.) was added during 5 min. while the temperature was kept at 45—50°. The mixture was stirred at 50° for 1 hr. during which it became homogeneous. It was then steam-distilled until no more formic acid came over, and the residue was extracted continuously with ethyl acetate to give 5β : 6α-*dihydroxy*bicyclo[2 : 2 : 1]*heptane-2α-carboxylic* 6α-*lactone* (XIII) (2·47 g., 88% from the acid; 2·02 g., 72% from the ester), m. p. 160° (Found: C, 62·4; H, 6·6. $C_8H_{10}O_3$ requires C, 62·3; H, 6·55%). Acetylation with acetic anhydride and pyridine gave 5β-*acetoxy*-6α-*hydroxy*bicyclo[2 : 2 : 1]*heptane-2α-carboxylic* 6α-*lactone* (XIV), m. p. 95—96° (from *iso*propyl ether) (Found: C, 61·45; H, 6·0. $C_{10}H_{12}O_4$ requires C, 61·2; H, 6·1%).

The hydroxy-lactone (XIII), m. p. and mixed m. p. 160°, was also obtained in high yield from the β-epoxide (XII; R = Me) by treatment with formic acid followed by isolation by the above procedure.

(*b*) A solution of the acetoxy-ether (XVII) (2·21 g.) in acetone (15 c.c.) was cooled to 5° and treated dropwise with 8N-chromic acid (15 c.c.) at <10°. It was then kept overnight at 20°, treated with sulphur dioxide and, after the addition of water, extracted with ether. Crystallisation from *iso*propyl ether gave the acetoxy-lactone (2·05 g., 89%), m. p. and mixed m. p. 95—96·5°.

Preparation of Methyl Ethers.—A solution of the unsaturated alcohol (V) (15 g.) in dry benzene (150 c.c.) containing potassium (20 g.) was stirred vigorously at 70—80° during 1·5 hr. while methyl iodide (50 g.) was added dropwise. The mixture was heated and stirred for a further 2 hr., then it was cooled to 0° and methanol (40 c.c.) was added cautiously to decompose the excess of potassium. Isolation with ether afforded 6α-*methoxy*bicyclo[2 : 2 : 1]*hept-2-ene* (14·1 g.), b. p. 76°/18 mm., n_D^{18} 1·4667 (Found: C, 77·2; H, 9·8. $C_8H_{12}O$ requires C, 77·4; H, 9·8%).

The alcohol (XV) (16 g.) was methylated similarly, to give bicyclo[2 : 2 : 1]*hept-5-en-2α-ylmethyl methyl ether* (15·1 g.), b. p. 138—140°/400 mm., n_D^{19} 1·4687 (Found: C, 78·0; H, 10·0. $C_9H_{14}O$ requires C, 78·2; H, 10·2%). These two ethers were used for some preliminary kinetic work (below).

Reaction Rates.—Bimolecular rate constants at 5° in benzene solution were determined for several of the unsaturated bicyclic compounds.

Compound	Initial concn. of compound (mole/l.)	Initial concn. of of BzO_2H (mole/l.)	k (mole^{-1} l. min.$^{-1}$)
(V)	0·0342	0·0707	0·121
(V; Me ether)	0·0352	0·07075	0·285
(V; acetate)	0·0345	0·07075	0·0592
(XV)	0·0365	0·0707	5·7 *
(XV; Me ether)	0·0349	0·07075	0·173
(XV; acetate)	0·0350	0·0708	0·127

* This relatively rapid reaction did not exactly follow a bimolecular law, the value of k decreasing with time. The value given is an approximate one computed after a reaction time of 2 min.

In respect of this and the following paper the authors are indebted to the Department of Scientific and Industrial Research for a Maintenance Grant (to B. N.), to Dr. G. D. Meakins for infrared spectra, and to Mr. E. S. Morton for most of the analyses.

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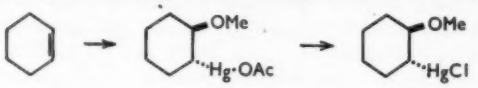
41. *Aspects of Stereochemistry. Part XII.* A Specific Directing Effect in the Mercuration of Some 4-Substituted* cyclo*Hexenes and* cis-*Hex-3-enol.*

By H. B. Henbest and B. Nicholls.

Functional groups can exert a directing effect on the stereochemistry of addition of HgX and OR at a double bond, in at least two ways. In the first, the reactions are completed by a suitably placed acid or alcohol group acting as an intramolecular nucleophile, and lactones or ethers are formed: some new examples are given in the *bicyclo*heptene series and with *trans*-hex-3-enol. A second, new directing effect [1] has been encountered with certain 4-substituted *cyclo*hexenes and *cis*-hex-3-enol: here hydroxyl or other Lewis base groups (OMe, OAc, CO_2Me, $CH_2{\cdot}OH$, CN) promote stereospecific addition of acetoxymercuri-groups and of anions (from solvent) to the double bond. A possible mechanism for these additions is discussed. As the mercuri-groups in these adducts can be removed by reduction, a two-step method for the specific addition of water or methanol to certain double bonds becomes available.

In continuation of our studies of the stereochemistry of addition of electrophilic reagents to olefinic bonds unsymmetrically located with respect to a substituent in the remainder of the molecule,[2,3] we have examined the reactions of some unsaturated compounds with mercuric acetate in methanol and, sometimes, water. Addition of mercuri-groups [4] was chosen in the hope that crystalline products would be obtained. Thus the symmetrical *cyclo*hexene gives a high yield of the crystalline adduct (I) on treatment with



(I) (II)

mercuric acetate in methanol. Anion-exchange takes place readily with compounds RHg·OAc, and aqueous sodium chloride converts the adduct (I) into the less soluble, more stable chloromercurial (II). Most of the adducts obtained in the present work were conveniently isolated as the chloromercuri-compounds by treatment of the final reaction solutions with sodium chloride. The *trans*-configuration of the *cyclo*hexene adduct (I) has been established by *X*-ray methods,[5] and the reaction may be envisaged as proceeding through some form of mercury cation [4,6] (further discussion below).

The present study began with some readily available 4-substituted *cyclo*hexenes and related *bicyclo*[2 : 2 : 1]heptenes. By the diene synthesis and other methods, a variety of compounds is available in each of which the substituent lies close enough to the double bond for electronic and/or steric effects to be expected.

Reactions with Substituted bicyclo[2 : 2 : 1]*Heptenes.*—A bromo-lactone is obtained from reaction of the unsaturated acid (III) with bromine,[7,8] and it was therefore not surprising to find that the chloromercuri-lactone (IV) was formed in high yield on treatment with mercuric acetate in methanol followed by anion-exchange with sodium chloride. Apart from the usual evidence, the structure (IV) was established by reduction of the

* Part XI, preceding paper.

[1] Cf. Henbest and Nicholls, *Proc. Chem. Soc.*, 1957, 61.
[2] Henbest and Wilson, *J.*, 1957, 1958.
[3] Henbest and Nicholls, *J.*, 1957, 4608.
[4] Cf. Review by Chatt, *Chem. Rev.*, 1951, **48**, 7.
[5] Brook and Wright, *Acta Cryst.*, 1951, **4**, 50.
[6] Lucas, Hepner, and Winstein, *J. Amer. Chem. Soc.*, 1939, **61**, 3102.
[7] Roberts, Trumbull, Bennett, and Armstrong, *ibid.*, 1950, **72**, 3116.
[8] ver Nooy and Rondestvedt, jun., *ibid.*, 1955, **77**, 3583.

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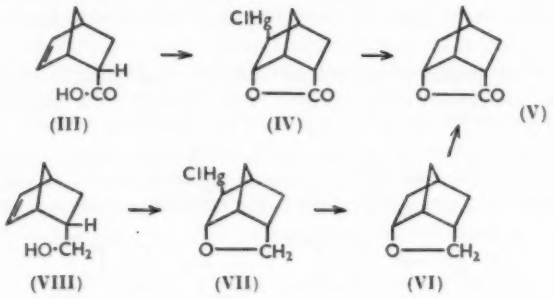
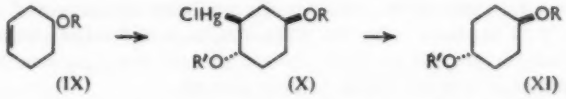
compound to the known [7,9] lactone (V) by sodium borohydride in ether–methanol, use of this reagent ensuring preservation of the lactone ring.

The related unsaturated alcohol (VIII) reacts analogously, the cyclic ether (VII) being formed. This product was reduced by hydrazine [10] to the cyclic ether [11] (VI), which was oxidised by chromic acid [12] to the lactone (V) obtained previously. [Most of the mercurials obtained in this work were reduced by the hydrazine procedure.[10] This method is convenient but with methoxy-mercurials obtained from substituted hexenes and *cyclo*hexenes reduction is accompanied by extensive regeneration of the double bond (see below).]

In the formation of the mercurials (IV and VII) the reactions are obviously completed by the neighbouring acid and alcohol groups which act as anion sources. Participation of these groups in the additions evidently precludes skeletal rearrangements such as are often encountered with other compounds of this series. A crystalline adduct has been obtained [13] from the reaction of the parent hydrocarbon, *bicyclo*[2 : 2 : 1]heptene, with mercuric acetate in methanol, but the published evidence does not distinguish between a rearranged or a non-rearranged structure for this product.



Reactions with 4-*Substituted* cyclo*Hexenes*.—In theory, four geometrical isomers can be obtained from a 4-substituted *cyclo*hexene by *trans*-addition of HgX and MeO groups, and at least three of them are formed when the 4-substituent is a methyl group.[14] However, it has now been found that with a 4-hydroxy-substituent (IX; R = OH) a single crystalline chloromercurial is obtained in 95% yield. Reductive removal of the chloromercuri-group gave the *trans*-1 : 4-diol methyl ether (XI; R = H, R′ = Me) (independent synthesis by partial methylation of the 1 : 4-diol), and the chloromercurial is therefore formulated as (X; R = H, R′ = Me).



The methoxymercuri-derivatives from the acetate (IX; R = Ac) and the methyl and benzyl ethers (IX; R = Me and CH_2Ph) were formed by addition in the same direction as the parent alcohol. From the acetate, both the acetoxymercuri- and the chloromercuri-compound (X; R = OAc, R′ = Me) were obtained crystalline, the structures being established by alkaline hydrolysis to the mercurial (X; R = H, R′ = Me). The adducts from the two ethers were liquid but were both reduced to *trans*-1 : 4-disubstituted compounds. Thus the adduct from the methyl ether gave *trans*-1 : 4-dimethoxy*cyclo*-

[9] Alder, Stein, Liebmann, and Rolland, *Annalen*, 1934, **514**, 197.
[10] Wright, *Canad. J. Chem.*, 1950, **30**, 268.
[11] Bruson and Riener, *Chem. Abs.*, 1948, **42**, 5471; U.S.P., 2,440,220.
[12] Cf. preceding paper.
[13] Rowland, *J. Amer. Chem. Soc.*, 1951, **73**, 2381.
[14] Park and Wright, *Canad. J. Chem.*, 1957, **35**, 1088.

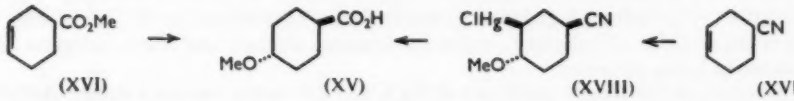
hexane (XI; R = R′ = Me) (independent synthesis), and that from the benzyl ether was reduced with hydrazine and then with lithium–ethylamine (removing the benzyl group) to give the *trans*-1 : 4-methoxy-alcohol (XI; R = H, R′ = Me).

Similar reactions in water gave the corresponding hydroxymercurials. The alcohol (IX; R = H) gave the crystalline mercurial (X; R = R′ = H) in high yield and this gave *trans*-quinitol (XI; R = R′ = H) on reduction with hydrazine. Similarly the liquid adduct from the methyl ether (IX; R = Me) was reduced to the *trans*-1 : 4-methoxy-alcohol (IX; R = Me, R′ = H), identical with that obtained by the alternative route described above.

Additions to the homologous unsaturated alcohol (XII; R = H) and its derivatives occur in the same stereochemical directions, adducts (XIII) being obtained. Thus the hydroxymercuri-product from the alcohol (XII; R = H) was reduced by hydrazine to the known *trans*-1 : 4-compound (XIV; R′ = H). The alcohol (XII; R = H), the acetate (XII; R = Ac), and the benzyl ether (XII; R = CH_2Ph) yielded similar crystalline methoxy-mercuri-adducts which were reduced to a single methoxy-alcohol. The 1 : 4-di-substituted structure (XIV; R′ = Me) for this methoxy-alcohol was confirmed by the fact that the α-naphthylurethane was identical with the lower-melting of the pair of

(XII) (XIII) (XIV) (XV)

isomers described earlier;[15] its *trans*-configuration is assigned by analogy with the reaction just described and by conversion of the adduct into the known methoxy-acid (XV) by chromic acid. This acid was also obtained from the unsaturated ester (XVI) by conversion into the methoxy-mercuri-adduct, reduction with hydrazine, and hydrolysis. Perhaps the most interesting finding in this series was that addition to the unsaturated nitrile (XVII) was also stereospecific, the crystalline adduct, formulated as (XVIII), being converted by hydrazine and hydrolysis into the same methoxy-acid (XV).



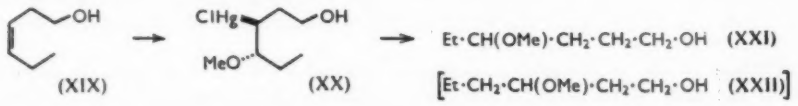
(XVI) (XV) (XVIII) (XVII)

The specificity of addition of HgX and the availability of many *cyclo*hexenes with a Lewis base substituent (see below) at the 4-position means that a variety of *trans*-1 : 4-substituted *cyclo*hexanes may now be synthesized by routes not always dependent on benzenoid starting materials. From the present work where hydrazine has been generally used for removal of the mercuri-group it appears that the overall introduction of a hydroxyl group by way of a hydroxy-mercuri-derivative gives a better yield than introduction of a methoxyl group by way of the methoxy-mercuri-derivative, the drawback in the latter series being that the methyl ethers from the reduction are accompanied by about equal amounts of unsaturated compounds formed by elimination of vicinal HgX and MeO groups.

Reactions with Hexenols.—We next examined the acylic analogue, *cis*-hex-3-enol (XIX). A liquid adduct was obtained whose infrared spectrum was similar to that of the previous cyclic product (X; R = H, R′ = Me) in that bands from hydroxyl and methoxyl groups were present. Reduction with hydrazine gave a methoxy-alcohol (together with *cis*-hex-3-enol), which appeared to be largely or wholly one compound, as judged by distillation and formation of a crystalline 4-diphenylylurethane in good yield. The methoxy-alcohol must be formulated as (XXI) or (XXII), the former being the product expected by analogy

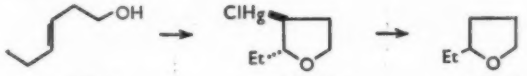
[15] Owen and Robins, *J.*, 1949, 326.

with the cyclic series. This was confirmed by exclusion, the isomeric methoxy-alcohol (XXII) being easier to synthesize by an unambiguous route. The hydroxy-ester obtained from a Reformatsky reaction between butyraldehyde and ethyl bromoacetate was methylated, and the methoxy-ester was then reduced with lithium aluminium hydride to the methoxy-alcohol (XXII), which gave a 4-diphenylylurethane different from that from the product from the mercuration sequence.



(XIX) (XX)

In contrast, the reaction of *trans*-hex-3-enol (XXIII) with mercuric acetate in methanol gave a liquid which did not show hydroxyl and methoxyl absorption in the infrared spectrum. Reduction of the product with hydrazine gave 2-ethyltetrahydrofuran (XXV), and the adduct may therefore be formulated as (XXIV; further comment on stereochemistry below), the hydroxyl group of the starting alcohol being involved as a nucleophilic component in the reaction as in the formation of the cyclic ether (VII) from the unsaturated alcohol (VIII).



(XXIII) (XXIV) (XXV)

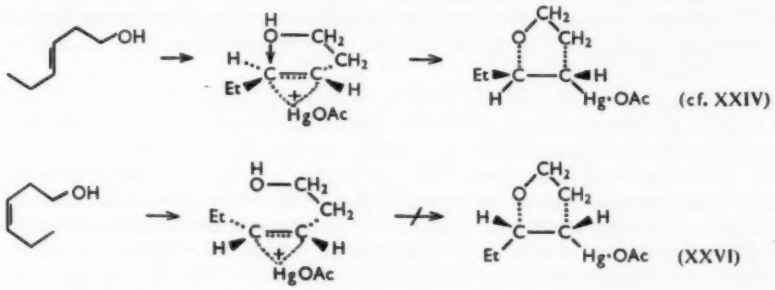
Discussion.—These results indicate that there are at least two mechanisms by which a substituent not directly linked to the unsaturated bond can cause unidirectional addition of HgX and OR. In the first, a functional group such as hydroxyl participates in the reaction as an internal nucleophile, and cyclic ethers or lactones are obtained. The formation of the ethers (VII) and (XXV) and the lactone (IV) provide examples, but many other instances, particularly formation of cyclic ethers, have been recorded before.[16] Participation of a hydroxyl group as a nucleophilic component is, of course, also well known in the addition of halogen to many unsaturated alcohols and acids, halogeno-ethers and -lactones being obtained.

In contrast, in the specific additions of HgX and OR to the various 4-substituted *cyclo*hexenes and to *cis*-hex-3-enol, the functional groups, although obviously exerting a directing effect, were unchanged at the end of the reaction. The choice between this second mechanism and the first mechanism depends on the structure of the unsaturated component. Thus the bicyclic olefinic alcohol (VIII) reacts by the first mechanism, the hydroxymethyl group being held relatively close to the α-side[12] of the double bond and the electrophilic mercuric salt approaching from the much less hindered β-side, circumstances favouring *trans*-addition. In its monocyclic analogue (XII; R = H) the chair-like ring system is flatter and less rigid; the first mechanism is less favoured and addition occurs by the second mechanism. [Reactions of these two unsaturated alcohols with perbenzoic acid also proceeded differently.[12]]

Formation of the tetrahydrofuran (XXIV) from *trans*-hex-3-enol by the first mechanism is not surprising. The flexible hydroxyethyl group can evidently move into the requisite position to complete the reaction as an anion source. The relative configurations of the ethyl and the chloromercuri-substituents in the product will be *trans* as shown (XXIV), if normal *trans*-addition to the olefinic bond takes place. This leads to an explanation for

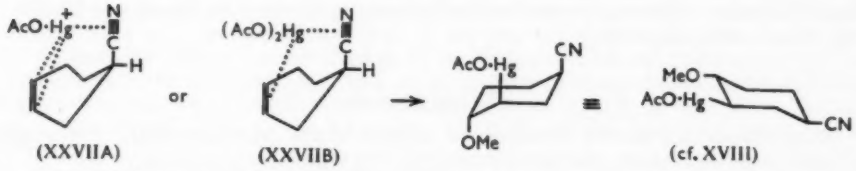
[16] Brook, Rodgman, and Wright, *J. Org. Chem.*, 1952, **17**, 988; Brook and Wright, *ibid.*, 1957, **22**, 1314; Nesmeyanov and Lutsenko, *Bull. acad. sci. U.R.S.S., Cl. sci. chim.*, 1943, 296, *Chem. Abs.*, 1944, **38**, 5498; Rosen, Ziegler, and Shabica, *J. Amer. Chem. Soc.*, 1955, **77**, 762; Summerbell and Lestina, *ibid.*, 1957, **79**, 3878.

the fact that *cis*-hex-3-enol did not give a substituted tetrahydrofuran by the first mechanism, for such a reaction would have given the isomer with the bulky ethyl and acetoxymercuri-groups in a very unfavourable eclipsed *cis*-arrangement (XXVI).



A more detailed picture of the second mechanism may be derived from the fact that in the *cyclo*hexene series compounds containing a Lewis base group (one or more unbonded electron pairs) at the 4-position undergo specific addition with final anion attack at the 1-position, to give products of the type (X, XIII, and XVIII), whereas 4-methyl*cyclo*hexene gives a mixture in which the predominant point of final anion attack has been the 2-position.[14] A partial explanation of the latter result may lie in inductive factors, and conversely it is possible that the electron-attracting properties of the Lewis base group could be responsible for final anion attack at the 1-position. However, the specificity of the formation of *trans*-1 : 4-substituted products seems to suggest that some extra factor is involved.

As the intermediate and reversible production of an organomercury salt complex (" mercurinium ion ") has been established [6] for the reaction between *cyclo*hexene and mercuric salts, it is now suggested that the presence of a Lewis base group at the 4-position may assist the formation of the complex in which the mercuric salt is held on the same side as the Lewis base group. For instance, in the reaction of 4-cyano*cyclo*hexene with mercuric



acetate in methanol, the formation of a *cis*-complex (*e.g.*, XXVIIA or B) may be assisted by π-electron donation from the nitrile group. [It may be noted that acetonitrile retards the rate of mercuration [17] and that a recent study [18] of the crystal structure of the complex $(NH_3)_4Pt(MeCN)_2$ has shown the nitrile groups to be bonded to platinum in a direction perpendicular to each C≡N bond.] Ultimate reaction of this *cis*-complex with methanol (axial attack) will give a triaxial structure which may be expected to revert to the tri-equatorial form of the observed product. The specific mercuration of *cis*-hex-3-enol may be explained similarly, a quasi-ring structure being built up in the intermediate complex.

One possible objection to the suggestion that a *cis*-intermediate (XXVII) may be involved in the present reactions is that the Lewis base group is required to be in a quasi-axial position. However the energy differences between the quasi-equatorial and the

[17] Birks and Wright, *J. Amer. Chem. Soc.*, 1940, **62**, 2412.
[18] Harris and Stephenson, *Chem. and Ind.*, 1957, 426.

quasi-axial 4-substituted conformations of *cyclo*hexene are probably in general much less than for the corresponding substituents in different *cyclo*hexane conformations. (Even in the latter series, reactions can take place sometimes from less favourable conformations.[3,19]) In a substituted *cyclo*hexane an axial substituent interacts sterically with two other axial groups. In a 4-substituted *cyclo*hexene, a quasi-axial group has only one other quasi-axial group with which to interact; the situation has been discussed before in greater detail.[20]

On the basis of previous evidence and on our interpretation of the *cis*- and *trans*-hex-3-enol results, we see no reason to doubt that addition of HgX and MeO or HO to unsaturated compounds is a typical electrophilic reaction in that *trans*-addition normally occurs.[4] Nevertheless doubts have been expressed[21] about the prevalence of *trans*-addition despite the apparent conclusiveness of the *X*-ray study of the *cyclo*hexene adduct.[5] These doubts apparently arise largely from an interpretation of the geometrical requirements of the general reaction of methoxy-mercurials in which the original double bond is regenerated on treatment of the adducts with mineral acid. For no very clear reasons a mechanism involving *cis*-removal of methoxy- and mercuri-groups has been favoured[21] for this type of elimination, with the consequence that, in a discussion of the addition of mercury derivatives to cinnamic acids and elimination from the adducts, the conclusion was drawn that *cis*-addition occurs. However it seems to us more likely that *trans*-addition generally takes place, and that the adducts are reconverted into the unsaturated compounds under acid conditions by an E_2 mechanism with the usual preference for a staggered *trans*-arrangement of groups to be eliminated. This general conclusion is supported by comparative kinetic studies[22] of the rates of formation of *cyclo*hexene from the *trans*-adduct (II) and from its *cis*-isomer.[23]

[*Added, October 23rd*, 1958.—Now that the stereochemical structure of *trans*-terpin has been settled (Barnes, *Austral. J. Chem.*, 1858, **11**, 134), the reactions of α-terpineol with mercuric salts can be seen to conform with the two mechanisms discussed above. According to the experimental conditions, either a mercurated cineole is formed by the first mechanism ($Me_2C{\cdot}OH$ being the internal nucleophile), or a mercurated *trans*-terpin is formed by the second mechanism. We consider therefore that this mercurated *trans*-terpin contains a *cis*-arrangement of HgX and $Me_2C(OH)$ groups, and that its isomer, formed by epimerization of the HgX group, must therefore have the mercuri-group *trans* to the $Me_2C{\cdot}OH$ group. This is a reversal of the previous suggestions by Brook and Wright (*J. Org. Chem.*, 1957, **22**, 1314).]

Experimental

Nomenclature and general directions are as given in the preceding paper. For many of the small-scale distillations, the bath-temperature only is given, as b. p. (b. t.).

General Procedure for the Addition of Mercury Compounds.—A solution of mercuric acetate (1 mol.) in methanol or water was added to the unsaturated compound, the mixture being shaken if necessary until it was homogeneous. It was then kept at approx. 20° until a test portion failed to give a precipitate of mercuric oxide on treatment with dilute aqueous sodium hydroxide (2—7 days). The solution, filtered if necessary from traces of mercurous salts, was usually treated with aqueous sodium chloride to give the chloromercuri-compound. With the reactions in methanol about two-thirds of the solvent was removed under reduced pressure before the addition of sodium chloride. For reduction of the mercurials, 90% hydrazine hydrate and a 3·2% w/v solution of sodium hydroxide in water were used.

[19] Turner, Mattox, Engel, McKenzie, McGuckin, and Kendall, *J. Biol. Chem.*, 1946, **162**, 565, 569, 571; Eliel, *Experientia*, 1953, **9**, 91; Noyce and Thomas, *J. Amer. Chem. Soc.*, 1957, **79**, 755.
[20] Corey and Sneen, *ibid.*, 1955, **77**, 2505.
[21] Wright, *Ann. New York Acad. Sci.*, 1957, **65**, 436.
[22] Professor S. Winstein, personal communication; T. G. Traylor, Thesis, University of California, Los Angeles, 1952.
[23] Romeyn and Wright, *J. Amer. Chem. Soc.*, 1947, **69**, 697.

Addition to bicyclo[2 : 2 : 1]*Hept-5-ene-2α-carboxylic Acid* (III).—The reaction solution from the acid (7·02 g.) and mercuric acetate (14·6 g.) in methanol (150 c.c.) was concentrated to 50 c.c. and treated with sodium chloride (3 g.) in water (20 c.c.). After being kept at 0° overnight, the product (17·1 g.) was collected. Crystallization from ethanol–ethyl acetate gave 5β-*chloromercuri*-6α-*hydroxy*bicyclo[2 : 2 : 1]*heptane*-2α-*carboxylic lactone* (IV), m. p. 222·5—224° (Found: C, 25·7; H, 2·3; MeO, 0. $C_8H_9O_2HgCl$ requires C, 25·75; H, 2·4; MeO, 0%). A similar experiment starting with the methyl ester (0·76 g.) of the unsaturated acid gave the same chloromercuri-lactone (1·51 g.), m. p. 222—224°.

For reduction, the organomercurial (17 g.) in ether–methanol (1 : 3; 50 c.c.) and sodium borohydride (3·8 g.) were heated under reflux for 3 hr. with stirring, and the organic product was then isolated with ether after the addition of hydrochloric acid. Crystallization from light petroleum gave the lactone (V) (5·8 g., 80%), m. p. 154—155° (lit., m. p. 155—156°). This lactone (identical m. p. and infrared spectrum) was also prepared by isomerization of the unsaturated acid with 50% sulphuric acid.[7,9]

Addition to bicyclo[2 : 2 : 1]*Hept-5-en-2α-ylmethanol* (VIII).—The reaction solution from the unsaturated alcohol (6·2 g.), mercuric acetate (16 g.), and methanol (150 c.c.) was concentrated to one-third bulk and treated with sodium chloride (3 g.) in water (20 c.c.). The precipitated 4β-*chloromercuri*-6-*oxa*tricyclo[3 : 2 : 1 : $1^{3:8}$]*nonane* (VII) (19 g.) had m. p. 227—229°. A sample recrystallized from benzene–light petroleum had m. p. 228—229° (Found: C, 26·6; H, 2·7; MeO, 0. $C_8H_{11}OHgCl$ requires C, 26·7; H, 3·1; MeO, 0%). Hydrazine hydrate (5 c.c.) was added to the organomercurial (10 g.) in sodium hydroxide solution (100 c.c.), and the mixture heated under reflux for 24 hr. Isolation with ether, sublimation under reduced pressure, and crystallization from ether–pentane gave 6-oxo*tricyclo*-[3 : 2 : 1 : $1^{3:8}$]nonane (VI) (3·03 g.), m. p. 102—106° (lit.,[11] m. p. 100—105°). Reduction of the organomercurial (7·2 g.) with lithium borohydride (1 g.) in boiling ether (200 c.c.) also gave this cyclic ether (1·54 g.), m. p. 100—106°. An authentic sample was prepared [11] by heating a mixture of the unsaturated alcohol (VIII) (4·27 g.) and dilute sulphuric acid (12·5 c.c. of concentrated acid in 75 c.c. of water) under reflux for 1 hr. Part of the product sublimed into the condenser but it was all collected into ether and crystallized as before, to give the product (3·67 g.), m. p. and mixed m. p. 102—106°.

For oxidation, the ether (VI) (1·3 g.) in acetone (5 c.c.) at 0° was treated with an 8N-solution (10 c.c.) of chromic acid in sulphuric acid at <15°. The mixture was kept overnight at 20°, the excess of reagent reduced with sulphur dioxide, and after the addition of water the product was isolated with ether. Sublimation under reduced pressure and crystallization from light petroleum afforded the lactone (V) (1·26 g.), m. p. and mixed m. p. 154—155·5°.

Methoxy-mercurial from cyclo*Hex*-3-*enol* (IX; R = H).—The reaction solution from the alcohol (7·4 g.) and mercuric acetate (23 g.) in methanol (300 c.c.) was concentrated to 70 c.c. and treated with sodium chloride (6 g.) in water (40 c.c.). After the mixture had been kept overnight at 0° the chloromercurial (26·5 g.), m. p. 159—161°, was collected. Crystallization from methanol gave 3β-*chloromercuri*-4α-*methoxy*cyclo*hexan*-1β-*ol* (X; R = H, R′ = Me), m. p. 161—162° (Found: C, 23·3; H, 3·6; OMe, 8·5. $C_7H_{13}O_2ClHg$ requires C, 23·0; H, 3·6; OMe, 8·5%).

The organomercurial (7·3 g.) in boiling sodium hydroxide solution (50 c.c.) was heated with hydrazine hydrate (2·5 c.c.) under reflux for 16 hr. Mercury (3·8 g., 95%) was formed and the product was isolated with ether. Distillation gave *cyclo*hex-3-enol (1·05 g., 52%), b. p. (b. t.) 93—103°/15 mm., n_D^{19} 1·4880, and 4α-*methoxy*cyclo*hexan*-1β-*ol* (XI; R = H, R′ = Me) (1·14 g., 40%), b. p. (b. t.) 115—122°/15 mm., n_D^{21} 1·4671 (Found: C, 64·5; H, 10·65. $C_7H_{14}O_2$ requires C, 64·6; H, 10·85%). The 3 : 5-dinitrobenzoate (90% yield) of the methoxy-alcohol had m. p. 130—134° (Noyce *et al.*[19] give m. p. 125·5—126·5°) (Found: C, 51·9; H, 4·75. Calc. for $C_{14}H_{14}O_7N_2$: C, 51·85; H, 4·95%). Oxidation of the methoxy-alcohol (0·5 g.) with 8N-chromic acid (0·98 c.c.) gave 4-methoxy*cyclo*hexanone (0·316 g., 63%), b. p. (b. t.) 100—110°/15 mm., n_D^{18} 1·4572 [2 : 4-dinitrophenylhydrazone, m. p. 144—144·5° (from benzene–light petroleum) (lit.,[24] m. p. 142·5—143·5°) (Found: C, 50·5; H, 5·2. Calc. for $C_{13}H_{16}O_5N_4$: C, 50·65; H, 5·25%)].

Hydroxy-mercurial from cyclo*Hex*-3-*enol* (IX; R = H).—The alcohol (5 g.) and mercuric acetate (15 g.) in water (150 c.c.) were shaken at room temperature for 10 days. Sodium chloride (3 g.) was added and the solution was evaporated to dryness under reduced pressure.

[24] Adkins and Rossow, *ibid.*, 1949, **71**, 3836.

The organomercurial (16·5 g., 94%) was extracted from the residue with ethanol. Crystallisation from benzene gave 3β-*chloromercuri*cyclo*hexane*-1β : 4α-*diol* (X; R = R′ = H), decomp. >150° (Found: C, 20·5; H, 2·9; Hg, 56·8. $C_6H_{11}O_2ClHg$ requires C, 20·5; H, 3·2; Hg, 57·1%).

Hydrazine hydrate (5 c.c.) was added to a boiling solution of the organomercurial (10·7 g.) in sodium hydroxide solution (85 c.c.), and the mixture was heated under reflux for 16 hr. The product was extracted with ethyl acetate and crystallised from acetone, to give *cyclo*hexane-1β : 4α-diol (2·95 g., 90%), m. p. 138·5—140° (dibenzoate, m. p. and mixed m. p. 150—151°) [lit.,[25] 140—141° and 149—150° respectively].

Methoxy-mercurial from cyclo*Hex*-3-*enyl Acetate* (IX; R = Ac).—The reaction solution from the acetate (5·6 g.), mercuric acetate (12·5 g.), and methanol (150 c.c.) was evaporated to dryness under reduced pressure. The residue was dissolved in the minimum quantity of ether and kept at 0° until the product (15·5 g., 90%) crystallized. Recrystallization from *iso*propyl ether gave 4β-*acetoxy*-2β-*acetoxymercuri*-1α-*methoxy*cyclo*hexane*, m. p. 96—98° (Found: C, 30·8; H, 4·1; OMe, 7·45. $C_{11}H_{18}O_5Hg$ requires C, 31·4; H, 4·2; OMe, 7·2%). Treatment of this compound (5 g.) in methanol (10 c.c.) with sodium chloride (1 g.) in water (10 c.c.) gave 4β-*acetoxy*-2β-*chloromercuri*-1α-*methoxy*cyclo*hexane* (X; R = Ac, R′ = Me) (4·7 g.), m. p. 111—113° (from benzene–light petroleum) (Found: C, 26·7; H, 3·7; OMe, 7·8. $C_9H_{15}O_3ClHg$ requires C, 26·55; H, 3·7; OMe, 7·6%).

A solution of the former mercurial (10·7 g.) in 5% aqueous sodium hydroxide (55 c.c.) was kept at 20° for 24 hr. Sodium chloride (2 g.) was added and carbon dioxide was passed in until the solution was neutral. The solid (8·95 g.) was crystallised from benzene, to give 3β-chloromercuri-4α-methoxy*cyclo*hexan-1β-ol, m. p. 161—162°, identical with the compound obtained from *cyclo*hex-3-enol.

4β-Acetoxy-2β-acetoxymercuri-1α-methoxy*cyclo*hexane (16·7 g.) with hydrazine hydrate (8 c.c.) in sodium hydroxide solution (150 c.c.) gave, after isolation with ether and distillation, *cyclo*hex-3-enol (1·76 g., 45%), b. p. 58—62°/15 mm., n_D^{21} 1·4861, and 4α-methoxy*cyclo*hexan-1β-ol (2·47 g., 50%), b. p. 100°/15 mm., n_D^{18} 1·4686 [3 : 5-dinitrobenzoate (90% yield), m. p. and mixed m. p. 130—134°].

Methoxy-mercurial from cyclo*Hex*-3-*enyl Methyl Ether* (IX; R = Me).—The reaction solution from the ether (5 g.) and methanolic 10% mercuric acetate (145 c.c.) was concentrated to one-third of its volume, and added to sodium chloride (3 g.) dissolved in water (20 c.c.); 2β-chloromercuri-1α : 4β-dimethoxy*cyclo*hexane (X; R = R′ = Me) (15·6 g.) separated as an oil. This mercurial (15 g.) with hydrazine hydrate (10 c.c.) in boiling sodium hydroxide solution (100 c.c.) gave *cyclo*hex-3-enyl methyl ether (1·55 g., 35%) and 1β : 4α-dimethoxy-*cyclo*hexane (XI; R = R′ = Me) (2·17 g., 38%), b. p. 88°/42 mm., n_D^{21} 1·4429 (lit.,[26] n_D^{18} 1·4430), whose infrared spectrum [27] was identical with that of an authentic sample prepared by methylation of the *trans*-diol.

Hydroxy-mercurial from cyclo*Hex*-3-*enyl Methyl Ether* (IX; R = Me).—Addition of sodium chloride (2·5 g.) in water (20 c.c.) to the reaction solution from the ether (4 g.) and mercuric acetate (11·5 g.) in water (100 c.c.) gave 2α-chloromercuri-4α-methoxy*cyclo*hexan-1β-ol (12·6 g.) as an oil. Reduction of the mercurial (10 g.) with hydrazine hydrate (10 c.c.) in aqueous sodium hydroxide solution (100 c.c.) yielded *cyclo*hex-3-enyl methyl ether (0·3 g., 10%), b. p. 30—34°/15 mm., n_D^{22} 1·4520, and 4α-methoxy*cyclo*hexan-1β-ol (2·81 g., 72%), b. p. 99—100°/15 mm., n_D^{22} 1·4655 [3 : 5-dinitrobenzoate (92% yield), m. p. and mixed m. p. 129—133°].

Methoxymercurial from Benzyl cyclo*Hex*-3-*enyl Ether* (IX; R = CH_2Ph).—The reaction solution from the benzyl ether (3·76 g.) and mercuric acetate (6·4 g.) in methanol (100 c.c.) was treated with sodium chloride (1·2 g.) in water (10 c.c.) to give 4β-benzyloxy-2β-chloromercuri-1α-methoxy*cyclo*hexane (8·52 g.) as a viscous oil. The mercurial (8 g.) was reduced with hydrazine hydrate (5 c.c.) and sodium hydroxide (1·9 g.) in water (60 c.c.). The product (isolated with ether) was dissolved in ethylamine (50 c.c.), cooled to 0°, and treated with finely chopped lithium (3 g.) during 30 min. The mixture was then shaken vigorously for 1 hr., and the product isolated with ether. Distillation gave *cyclo*hexanol (1·03 g., 58%), b. p. (b. t.) 100—105°/21 mm., n_D^{21} 1·4671, and 4α-methoxy*cyclo*hexan-1β-ol (0·94 g., 32%) b. p. (b. t.) 110—115°/16 mm., n_D^{21} 1·4670 (3 : 5-dinitrobenzoate, m. p. and mixed m. p. 130—134°).

Methoxy- and Hydroxy-mercurial from cyclo*Hex*-3-*enylmethanol* (XII; R = H).—The

[25] Owen and Robins, *J.*, 1949, 320.
[26] Palfray and Sabetay, *Bull. soc. chim.*, 1928, **43**, 895.
[27] Henbest, Meakins, Nicholls, and Wagland, *J.*, 1957, 1462.

reaction solution from the alcohol (11·24 g.) and mercuric acetate (32 g.) in methanol (250 c.c.) was evaporated to 100 c.c. and treated with sodium chloride (6 g.) in water (50 c.c.). The precipitated gum slowly crystallized (36 g.; m. p. 130—135°). The pure 3β-*chloromercuri*-4α-*methoxy*-1β-cyclo*hexylmethanol* (XIII; R = H, R′ = Me) had m. p. 135—140° (from methanol) (Found: C, 25·45; H, 3·75. $C_8H_{15}O_2ClHg$ requires C, 25·35; H, 4·0%). The mercurial (30 g.) was reduced by hydrazine to *cyclo*hex-3-enylmethanol (5·29 g., 59%), b. p. 84—86°/14 mm., n_D^{22} 1·4807, and 4α-*methoxy*-1β-cyclo*hexylmethanol* (XIV; R′ = Me) (4·0 g., 32%), b. p. 110—111°/14 mm., n_D^{23} 1·4684 (Found: C, 66·4; H, 11·0. $C_8H_{16}O_2$ requires C, 66·65; H, 11·2%). The α-naphthylurethane separated from ligroin as needles, m. p. and mixed m. p. with an authentic sample,[28] 94—96° (Found: C, 73·3; H, 7·3. Calc. for $C_{19}H_{23}O_3N$: C, 72·8; H, 7·4%). Oxidation of the methoxy-alcohol with chromic acid in acetone gave a good yield of the *trans*-methoxy-acid, m. p. 55·5—58·5° (anilide, m. p. 180—183°) (see below).

The reaction solution from the unsaturated alcohol (5·61 g.) and mercuric acetate (16·1 g.) in water (200 c.c.) was treated with sodium chloride (3·5 g.) in water (20 c.c.), 2α-*chloromercuri*-4α-*hydroxymethyl*cyclo*hexan*-1β-*ol* (XIII; R = R′ = H) (17·2 g.), m. p. 170—172°, being precipitated. The pure compound had m. p. 179—181° (from methanol–*iso*propyl ether) (Found: C, 22·95; H, 3·7. $C_7H_{13}O_2ClHg$ requires C, 23·0; H, 3·6%). Reduction of the mercurial (15·1 g.) with hydrazine gave 4α-hydroxymethyl*cyclo*hexan-1β-ol (XIV; R′ = H) (3·47 g., 65%), m. p. 95—97·5°. The pure diol had m. p. and mixed m. p. with an authentic sample,[28] 100—102° (lit.,[25] m. p. 103°).

Methoxy-mercurial from cyclo*Hex*-3-*enylmethyl Acetate* (XII; R = Ac).—Addition of sodium chloride (3·5 g.) in water (20 c.c.) to the reaction solution from the unsaturated acetate (7·69 g.) and mercuric acetate (16 g.) in methanol (150 c.c.) gave 3β-*chloromercuri*-4α-*methoxy*-1β-cyclo*hexylmethyl acetate* (XIII; R = Ac, R′ = Me) (19·5 g.). The pure compound had m. p. 94—96° (from methanol) (Found: C, 28·2; H, 3·9. $C_{10}H_{17}O_3ClHg$ requires C, 28·5; H, 4·05%). Reduction o the mercurial (15 g.) by the hydrazine method yielded *cyclo*hex-3-enylmethanol (2·13 g.; 53%), b. p. (b. t.) 100—105°/14 mm., n_D^{19} 1·4820 and 4α-methoxy*cyclo*hexyl-1β-carbinol (1·89 g.; 37%), b. p. (b. t.) 126—130°/14 mm., n_D^{20} 1·4707 (α-naphthylurethane, m. p. and mixed m. p. 94·5—96°).

Methoxy-mercurial from Benzyl cyclo*Hex*-3-*enylmethyl Ether* (XII; R = CH_2Ph).—The reaction solution from the benzyl ether (9·99 g.) and mercuric acetate (16 g.) in methanol (300 c.c.) was treated with an excess of aqueous sodium chloride to give *benzyl* 3β-*chloromercuri*-4α-*methoxy*-1β-cyclo*hexylmethyl ether* (XIII; R = CH_2Ph, R′ = Me) (23·4 g.), m. p. 75—79°. The pure mercurial had m. p. 77—81° (Found: C, 37·9; H, 4·1. $C_{15}H_{21}O_2ClHg$ requires C. 38·4; H, 4·5%). The mercurial (17 g.) was reduced with hydrazine in the usual way. The product was isolated with ether and dissolved in ethylamine (75 g.), and finely chopped lithium (5 g.) was added in portions with external cooling to moderate the reaction. Isolation in the usual way gave *cyclo*hexylmethanol (2·5 g., 60%), b. p. (b. t.) 100—102°/13 mm., n_D^{19} 1·4827, and 4α-methoxy-1β-*cyclo*hexylmethanol (0·78 g., 14%), b. p. (b. t.) 135—140°/13 mm., n_D^{21} 1·4711 (α-naphthylurethane, m. p. and mixed m. p. 94—96°).

Methoxy-mercurial from Methyl cyclo*Hex*-3-*enecarboxylate* (XVI).—The reaction solution from the unsaturated ester (13·9 g.) and mercuric acetate (30 g.) in methanol (300 c.c.) was concentrated to one-third of its bulk and treated with sodium chloride (6 g.) in water (30 c.c.), to give the mercurial (37·5 g.) as a gum. Reduction of the mercurial (30 g.) by the hydrazine method gave *cyclo*hex-3-enecarboxylic acid (5·84 g., 58%), b. p. 59—60°/0·1 mm., n_D^{21} 1·4789, and crude methoxy-acid (3·63 g., 30%) which partially crystallized. Further crystallization from light petroleum gave pure 4α-methoxy*cyclo*hexane-1β-carboxylic acid (XV), m. p. and mixed m. p. (see below) 55·5—58·5°. More methoxy-acid was recovered as its anilide, m. p. 181—182·5° (see below), from the mother-liquors.

Methoxy-mercurial from 4-*Cyano*cyclo*hexene* (XVII).—The reaction solution from the nitrile (11·2 g.) and mercuric acetate (32 g.) in methanol (300 c.c.) was concentrated to 100 c.c. and treated with sodium chloride (6 g.) in water (60 c.c.) to precipitate the mercurial (35·5 g.), m. p. 107—113°. Crystallization from benzene–*iso*propyl ether gave 2β-*chloromercuri*-4β-*cyano*-1α-*methoxy*cyclo*hexane* (XVIII), m. p. 125—129° (Found: C, 25·5; H, 3·4. $C_8H_{12}ONClHg$ requires C, 25·65; H, 3·2%).

The mercurial (30 g.) was reduced with hydrazine hydrate (10 c.c.) in boiling sodium

[28] Kindly provided by Dr. L. N. Owen (Imperial College).

XUM

hydroxide solution (200 c.c.) during 16 hr. Sodium hydroxide (18 g.) was added and the solution heated under reflux for a further 24 hr. to ensure hydrolysis of the nitrile. Isolation with ether and distillation gave *cyclo*hex-3-enecarboxylic acid (4·8 g., 48%), b. p. 83—84°/0·6 mm., n_D^{23} 1·4774, and 4α-methoxy*cyclo*hexane-1β-carboxylic acid (XV) (5·72 g., 45%), b. p. 100°/0·1 mm., m. p. 56—59° (from light petroleum) (lit.,[29] 59—60°) (Found: C, 61·1; H, 8·9. Calc. for $C_8H_{14}O_3$: C, 60·75; H, 8·9%). The anilide of this acid separated from benzene–light petroleum as needles, m. p. 181—183° (lit.,[29] 186—186·5°) (Found: C, 72·1; H, 8·2. Calc. for $C_{14}H_{19}O_2N$: C, 72·05; H, 8·2%).

Methoxy-mercurial from cis-*Hex*-3-*enol* (XIX).—The reaction mixture from the alcohol (7·2 g.), mercuric acetate (23 g.), and methanol (150 c.c.) was concentrated to 50 c.c. and treated with sodium chloride (4·5 g.) in water (20 c.c.), the mercurial (XX) (22·5 g.) separating as an oil. Reduction of the mercurial (11·9 g.) with hydrazine hydrate (5 c.c.) in sodium hydroxide solution (100 c.c.) gave *cis*-hex-3-enol (1·32 g., 40%), b. p. 69—74°/24 mm., n_D^{19} 1·4418, and 4-*methoxyhexan*-1-*ol* (XXI) (2·07 g., 48%), b. p. 100—101°/24 mm., n_D^{19} 1·4345 (Found: C, 63·4; H, 11·9. $C_7H_{16}O_2$ requires C, 63·6; H, 12·2%). Its 4-*diphenylylurethane* had m. p. 65—67° (from ligroin) (Found: C, 73·4; H, 7·6. $C_{20}H_{25}O_3N$ requires C, 73·35; H, 7·7%): this m. p. was depressed to 52—54° on admixture with the derivative from 3-methoxyhexan-1-ol (see below).

Mercurial from trans-*Hex*-3-*enol* (XXIII).—The reaction solution from the alcohol (5 g.) and mercuric acetate (16 g.) in methanol (300 c.c.) was concentrated to 70 c.c. and treated with sodium chloride (3 g.) in water (20 c.c.), to give 3β-chloromercuri-2α-ethyltetrahydrofuran (XXIV) (13·8 g.). For reduction, the chloromercurial (10·5 g.) in boiling sodium hydroxide solution (150 c.c.) was treated with hydrazine hydrate (10 c.c.), the mixture then being heated under reflux for 16 hr. Distillation yielded 2-ethyltetrahydrofuran (XXV) (1·27 g., 42%), b. p. 107—108°/755 mm., n_D^{18} 1·4175 (lit., b. p. 108·5°/759 mm., n_D^{20} 1·4170), and *trans*-hex-3-enol (1·56 g., 42%), b. p. 150—152°/755 mm., n_D^{17} 1·4393. For comparison of the infrared spectrum, an authentic sample of 2-ethyltetrahydrofuran (1·46 g., 73%) was prepared by slowly heating *trans*-hex-3-enol (1·98 g.) and concentrated sulphuric acid (0·2 g.) to 150°.

Preparation of 3-*Methoxyhexan*-1-*ol* (XXII).—A mixture of *n*-butyraldehyde (70 g.) and ethyl bromoacetate (160 g.) was added to activated zinc dust (60 g.) in benzene (1 l.), with cooling. Isolation in the usual way gave the hydroxy-ester (92·7 g., 58%), b. p. 90—92°/14 mm., n_D^{23} 1·4278 (lit., b. p. 83—85°/10 mm.). A mixture of the hydroxy-ester (20·1 g.), methyl iodide (70 g.), and ether (50 c.c.) was stirred and heated under reflux while silver oxide (36 g.) was added in 1 g. portions during several hours. Heating and stirring were continued for 12 hr. and the product was isolated as usual, to yield *ethyl* 3-*methoxyhexanoate* (16·3 g., 75%), b. p. 80—82°/14 mm., n_D^{21} 1·4201 (Found: C, 61·8; H, 10·55. $C_9H_{18}O_3$ requires C, 62·05; H, 10·4%), and unchanged hydroxy-ester (3·3 g.), b. p. 88—92°/15 mm., n_D^{21} 1·4270.

A solution of the methoxy-ester (11·1 g.) in dry ether (50 c.c.) was added dropwise to a stirred suspension of lithium aluminium hydride (5 g.) in ether (100 c.c.), the mixture then being heated under reflux for 2 hr. Isolation as usual gave 3-*methoxyhexan*-1-*ol* (7·46 g., 90%), b. p. 84°/15 mm., n_D^{21} 1·4279 (Found: C, 63·85; H, 12·05. $C_7H_{16}O_2$ requires C, 63·6; H, 12·2%). Its 4-*diphenylylurethane* had m. p. 47—52° (from light petroleum) (Found: C, 73·25; H, 7·5. $C_{20}H_{25}O_3N$ requires C, 73·35; H, 7·7%).

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[29] Noyce and Weingarten, *J. Amer. Chem. Soc.*, 1957, **79**, 3093.

42. *Studies on the Diels–Alder Reaction. Part V.*[1] *Further Transformation Products of* cis-syn-1 : 2 : 3 : 4 : 5 : 6 : 12 : 13 : 14 : 15-*Decahydro-8-methoxy*-1 : 4-*dioxochrysene.*

By P. A. Robins and James Walker.

Equilibration of *cis-syn*-1 : 2 : 3 : 4 : 5 : 6 : 12 : 13 : 14 : 15-decahydro-8-methoxy-1 : 4-dioxochrysene (I) on alkaline alumina afforded a mixture of the *trans-anti*- (II) and the (*?*)*trans-syn*-stereoisomer (V), both of which, like (I), were converted into a mixture of *cis*-1 : 2 : 3 : 4 : 5 : 6 : 11 : 12 : 13 : 14-decahydro-8-methoxy-1 : 4-dioxochrysene (VI) and 5 : 6 : 11 : 12-tetrahydro-1 : 8-dimethoxychrysene (VII; R = Me) by hydrochloric acid in methanol. The *trans-anti*-diketone (II) has been converted into the *trans-anti-cis*- (III) and *trans-anti-trans*-dodecahydro-diketone (IV), and further correlations of stereochemical configuration have been made *via* the $C_{(1)}$-monoketal (IX) of the diketone (I). The formation from compounds having a *trans*-fusion of rings C and D of substances with a *cis*-fusion of these two rings during reactions in which an olefinic double bond migrates from the 11 : 16- to the 15 : 16-position is interpreted in terms of prototropic lability of the products and stereoelectronic kinetic control of ketonisation of derived enols.

In Part IV[1] the preparation of *cis-syn*-1 : 2 : 3 : 4 : 5 : 6 : 12 : 13 : 14 : 15-decahydro-8-methoxy-1 : 4-dioxochrysene (I) was described, and a series of transformation products, mostly of the *cis-syn*-configuration, was characterised and interrelated; the ready migration of the 11 : 16-double bond into the 15 : 16-position in the presence of mineral acid was also noted. In the present communication we describe a further series of transformation products derived from the diketone (I), to which access has been gained by stereochemical inversions at points of ring-fusion rendered labile by the presence of adjacent carbonyl groups, effected in such a manner as to permit logical assignment of stereochemical configurations to the resulting products. Starting from the same *cis-syn*-diketone (I) a new and stereoselective total synthesis of œstrone has also been developed and is outlined elsewhere.[2]

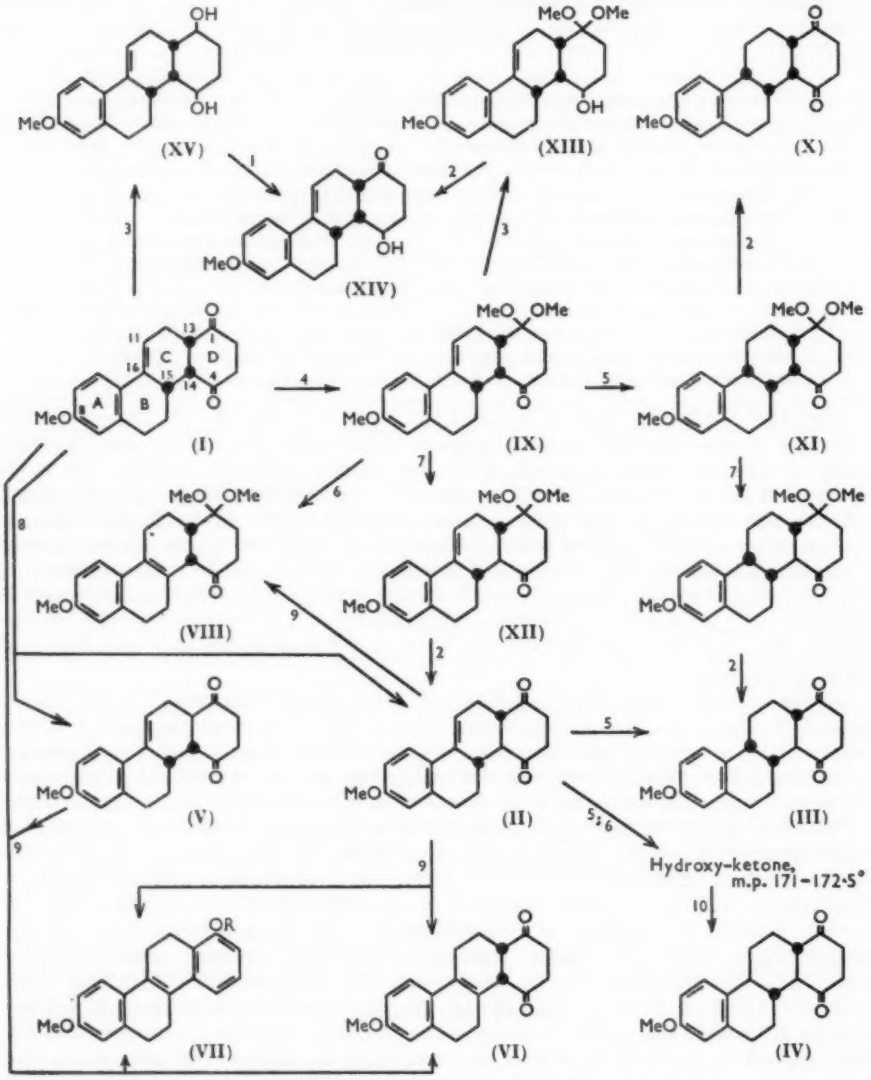
On the analogy of experience gained in the hydrophenanthrene series,[3] stereoisomerisation of *cis-syn*-1 : 2 : 3 : 4 : 5 : 6 : 12 : 13 : 14 : 15-decahydro-8-methoxy-1 : 4-dioxochrysene (I) was effected by passage in benzene solution down a column of alkaline activated alumina. Elution with benzene–chloroform gave a mixture of one major and one minor component, which could be separated by crystallisation. These two products had identical ultraviolet light absorption spectra with maxima at 262 and 294—295 mμ, indicating retention of the olefinic double bond in the 11 : 16-position;[1] these spectra, however, showed significant hypsochromic shifts of the maxima in comparison with those of the starting material (I), and a discussion of these and similar hypsochromic shifts and of their relation to changes in stereochemistry will be incorporated in another communication. That the major component was the expected *trans-anti*-stereoisomer (II) was confirmed by its conversions into *trans-anti-cis*- (III) and *trans-anti-trans*-1 : 2 : 3 : 4 : 5 : 6 : 11 : 12 : 13 : 14 : 15 : 16-dodecahydro-8-methoxy-1 : 4-dioxochrysene (IV), while the minor component was probably the *trans-syn*-stereoisomer (V), which appears on the basis of qualitative conformational analysis to be more stable than the alternative *cis-anti*-form. No chemical evidence for the *trans-syn*-configuration of the minor product could be obtained as insufficient material was available for a detailed study.

Treatment of *trans-anti*-1 : 2 : 3 : 4 : 5 : 6 : 12 : 13 : 14 : 15-decahydro-8-methoxy-1 : 4-dioxochrysene (II) with methanol and hydrochloric acid in a manner similar to that described previously[1] for the *cis-syn*-stereoisomer (I) afforded the *same* products as were

[1] Part IV, Robins and Walker, *J.*, 1956, 3249.
[2] Cole, Johnson, Robins, and Walker, *Proc. Chem. Soc.*, 1958, 114.
[3] Part III, Robins and Walker, *J.*, 1954, 3960.

XUM

formed from the latter, namely, *cis*-1 : 2 : 3 : 4 : 5 : 6 : 11 : 12 : 13 : 14-decahydro-8-methoxy-1 : 4-dioxochrysene (VI) and 5 : 6 : 11 : 12-tetrahydro-1 : 8-dimethoxychrysene (VII; R = Me).[1,4] The *same* products, (VI) and (VII; R = Me), were also obtained on similar



treatment of the presumed *trans-syn*-stereoisomer (V). When the *trans-anti*-stereoisomer (II) was similarly treated with ethanol and propan-1-ol in the presence of hydrochloric acid the main products isolated were the respective 1-alkoxy-5 : 6 : 11 : 12-tetrahydro-8-methoxychrysenes (VII; R = Et, Pr^n) formed by aromatisation in the manner described in

[4] Robins and Walker, *J.*, 1956, 3260.

recent communications.[4,5] Under the conditions of the ready ketal formation which we have previously described,[4,5] namely, treatment with hot methanol containing a mere trace of hydrogen chloride, the *trans-anti*-diketone (II) afforded the *cis*-ketal, *cis*-1 : 2 : 3 : 4 : 5 : 6 : 11 : 12 : 13 : 14-decahydro-1 : 1 : 8-trimethoxy-4-oxochrysene (VIII), previously obtained[4] from the *cis-syn*-stereoisomer (I). The formation of compounds with a *cis*-fusion from substances having a *trans*-fusion of rings C and D in these experiments is discussed below.

Catalytic hydrogenation of the *trans-anti*-diketone (II) under neutral conditions with palladium and platinum catalysts gave a more complex (or less readily separable) mixture than that obtained from the corresponding compound in the analogous perhydrophenanthrene series.[3] The main component obtained on hydrogenation interrupted after absorption of 1 mol. of hydrogen was a diketone, m. p. 171—174°, which was separated by crystallisation. This diketone, which is subsequently shown to be *trans-anti-cis*-1 : 2 : 3 : 4 : 5 : 6 : 11 : 12 : 13 : 14 : 15 : 16-dodecahydro-8-methoxy-1 : 4-dioxochrysene (III), was unstable to passage in solution down a column of alkaline alumina, giving a mixture which could not be separated by crystallisation; further catalytic hydrogenation also gave a mixture inseparable by crystallisation.

Two further components of the mixture obtained by neutral hydrogenation to completion of the *trans-anti*-diketone (II) were separated by chromatography on alumina. Each was a dodecahydro-hydroxy-ketone, as shown by the presence of both hydroxyl and carbonyl absorption bands in their infrared spectra and anisole-type ultraviolet light absorption spectra. One, m. p. 171—172·5°, on oxidation with chromium trioxide in acetic acid at room temperature gave in poor yield a diketone, m. p. 181—184°, differing from the *trans-anti-cis*-diketone (III) described above. The hydroxy-ketone, m. p. 171—172·5°, which gave a toluene-*p*-sulphonyl derivative under mild conditions, was probably *trans-anti-trans*-1 : 2 : 3 : 4 : 5 : 6 : 11 : 12 : 13 : 14 : 15 : 16-dodecahydro-4-hydroxy-8-methoxy-1-oxochrysene, in analogy with the behaviour observed in the perhydrophenanthrene series,[3] and the diketone obtained from it must have been *trans-anti-trans*-1 : 2 : 3 : 4 : 5 : 6 : 11 : 12 : 13 : 14 : 15 : 16-dodecahydro-8-methoxy-1 : 4-dioxochrysene (IV). The second hydroxy-ketone, m. p. 181—185°, gave no recognisable product on oxidation with chromium trioxide in acetic acid at room temperature, and, on a number of occasions, similar oxidations have failed, possibly owing to attack by the oxidising agent at the highly reactive 6- and 16-carbon atoms. Indeed, in an attempt to hydrogenate the *trans-anti*-diketone (II) in acetic acid with a platinum catalyst and then to re-oxidise the resultant mixture of diols with chromium trioxide in acetic acid, the only product isolated was a small quantity of a compound giving analytical figures suggesting the formula $C_{19}H_{20}O_5$, and showing a strong infrared carbonyl absorption band at 1770 cm.$^{-1}$ besides the expected one at 1710 cm.$^{-1}$, and a hydroxyl absorption band at *ca.* 3380 cm.$^{-1}$.

cis-syn-1 : 2 : 3 : 4 : 5 : 6 : 12 : 13 : 14 : 15-Decahydro-1 : 1 : 8-trimethoxy-4-oxochrysene (IX), the preparation of which by the action of methanol and acetic acid on the corresponding *cis-syn*-diketone (I) is described elsewhere,[2] has been a useful starting-point for providing proof of the configurations assigned to some of the compounds described above. On attempted catalytic hydrogenation of the trimethoxy-ketone (IX) in solution in ethyl acetate in the presence of either palladium or platinum catalysts in various forms absorption of hydrogen ceased before the theoretical volume required for saturation of the double bond had been taken up, and ultraviolet spectrophotometric examination of the crude product indicated the occurrence of double-bond migration to the extent of between 41 and 84%; this was confirmed by the isolation of the isomeric *cis*-1 : 2 : 3 : 4 : 5 : 6 : 11 : 12 : 13 : 14-decahydro-1 : 1 : 8-trimethoxy-4-oxochrysene (VIII). When, however, methanol was used as solvent, the starting material (IX) being relatively insoluble, hydrogenation at a supported palladium catalyst was rapid and complete, as was shown by the ultraviolet

[5] Robins and Walker, *J.*, 1957, 177.

light absorption spectrum of the crude product. The product failed to crystallise, but on storage for prolonged periods in contact with methanol or, more rapidly, on treatment with warm acetic acid gave the known [1] *cis-syn-cis*-1 : 2 : 3 : 4 : 5 : 6 : 11 : 12 : 13 : 14 : 15 : 16-dodecahydro-8-methoxy-1 : 4-dioxochrysene (X). Equilibration of crude *cis-syn-cis*-1 : 2 : 3 : 4 : 5 : 6 : 11 : 12 : 13 : 14 : 15 : 16-dodecahydro-1 : 1 : 8-trimethoxy-4-oxochrysene (XI) with boiling methanolic potassium hydroxide again gave a non-crystalline product, but brief treatment with warm acetic acid afforded the expected crystalline *trans-anti-cis*-1 : 2 : 3 : 4 : 5 : 6 : 11 : 12 : 13 : 14 : 15 : 16-dodecahydro-8-methoxy-1 : 4-dioxochrysene (III), identical with, and confirming the stereochemical configuration of, the diketone obtained as described above by hydrogenation of the *trans-anti*-diketone (II); this experiment also confirms the *trans-anti*-configuration of the diketone (II) itself.

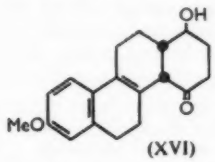
Equilibration of the *cis-syn*-trimethoxy-ketone (IX) itself with boiling alcoholic alkali (or under a variety of other alkaline enolising conditions) gave a mixture, which, from its ultraviolet light absorption spectrum ($\lambda_{max.}$ 264 and 293—298 mμ), must have contained a substantial amount of the *trans-anti*-stereoisomer (XII) of the starting material (IX). Repeated crystallisation of the mixture, however, gave only a small amount of the starting material (IX), and no other pure component could be isolated. After mild treatment with warm acetic acid the resultant mixture of diketones was separated more readily into the relatively insoluble *cis-syn*-diketone (I) and the more soluble *trans-anti*-stereoisomer (II), identical with that obtained above by stereoisomerisation of the *cis-syn*-form (I) with alkaline alumina, this confirmed the assigned *trans-anti*-configuration, since in the experiment just described only the 4-carbonyl group is available to effect stereochemical equilibration by enolisation.

Reduction with lithium aluminium hydride of the *cis-syn*-trimethoxy-ketone (IX) afforded, provided that care was taken in the subsequent working up to prevent hydrolysis of the ketal group or migration of the olefinic double bond, *cis-syn*-1 : 2 : 3 : 4 : 5 : 6 : 12 : 13 : 14 : 15-decahydro-4-hydroxy-1 : 1 : 8-trimethoxychrysene (XIII) which was converted by brief treatment with warm acetic acid into the known [1] *cis-syn*-hydroxy-ketone (XIV); this experiment further identifies conclusively as the compound (XIV) the product of the oxidation [1] by the Oppenauer method of the diol (XV) obtained by reduction of the *cis-syn*-diketone (I) with lithium aluminium hydride. The hydroxy-trimethoxy-compound (XIII) failed to give a toluene-*p*-sulphonyl derivative under mild conditions, and the 4-hydroxyl group is therefore presumably axial, as it was also not attacked in the Oppenauer oxidation, while the 1-hydroxyl group in the diol (XV) is obviously equatorial; these stereochemical relations are precisely analogous to those obtaining in the corresponding compound in the hydrophenanthrene series.[3]

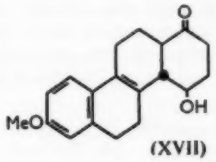
A noteworthy feature of the stereochemical transformations recorded in the present communication is the repeated occurrence of the formation from a compound having a *trans*-fusion of rings C and D of a substance with a *cis*-fusion of these two rings during reactions in which an olefinic double bond migrates from the 11 : 16- into the 15 : 16-position. Thus, the *trans-anti*- (II) and (?)*trans-syn*-diketone (V) having the olefinic double bond in the 11 : 16-position are both converted by suitable treatment with methanolic hydrochloric acid into the *cis*-diketone (VI) with the olefinic double bond in the 15 : 16-position, while ketal formation by the 1-carbonyl group of the *trans-anti*-diketone (II) affords the *cis*-trimethoxy-ketone (VIII). To these observations one may add the fact that *cis*-1 : 2 : 3 : 4 : 5 : 6 : 11 : 12 : 13 : 14-decahydro-1-hydroxy-8-methoxy-4-oxochrysene (XVI) is stable to attempted stereoisomerisation with perchloric acid in ethyl acetate (and is largely decomposed by alkaline reagents),[1] but it should be pointed out that an additional factor opposing *cis* ⟶ *trans* conversion in this instance is the need for the equatorial 1-hydroxyl group in the *cis*-form to assume an axial position in the *trans*-stereoisomer. In contrast with these observations is the fact that *cis-syn*-decahydro-4-hydroxy-8-methoxy-1-oxochrysene (XIV), although, contrary to expectation, found not to have undergone stereochemical inversion at $C_{(13)}$ during its formation in the Oppenauer

oxidation of the *cis-syn*-diol (XV), passed readily on treatment with alcoholic hydrochloric acid into the *trans*-hydroxy-ketone (XVII), and the same *trans*-hydroxy-ketone (XVII) was formed directly in the Oppenauer oxidation of the *cis*-diol (XVIII).[1]

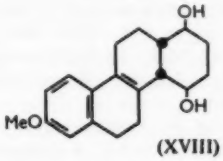
The apparently anomalous products are therefore seen to have the olefinic double bond in the 15 : 16-position and to have a carbonyl group at $C_{(4)}$. This system (XIX) would be expected to be a highly labile prototropic system with the position of equilibrium [6] entirely



(XVI)



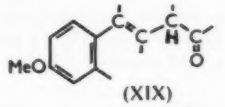
(XVII)



(XVIII)

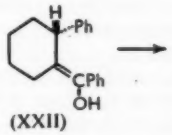
in favour of the $\Delta^{\beta\gamma}$-form and it should show a strong tendency to enolise, comparable, in fact, with that of ω-styrylacetophenone (XX), which enolises readily and whose enol ketonises rapidly.[7]

We are therefore concerned with the stereochemistry of the ketonisation of the enolic forms (XXI) of compounds (VI), (VIII), and (XVI), and the situation here is analogous to

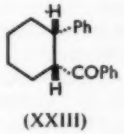


(XIX)

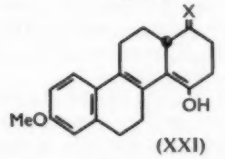
Ph·CH=CH·CH$_2$·COPh
(XX)



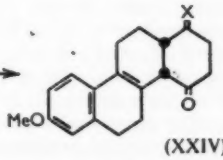
(XXII)



(XXIII)



(XXI)



(XXIV)

the cases discussed by Zimmerman,[8] who observed ketonisation of suitably constituted enols to give the thermodynamically less stable form of the related ketone; for example, the enolic form (XXII) of 1-benzoyl-2-phenyl*cyclo*hexane ketonises to give the *cis*-compound (XXIII) with complete stereospecificity. Similar stereoelectronic kinetic control of ketonisation to that operating in Zimmerman's example would favour in the present cases the formation from the enols (XXI) of the thermodynamically less stable *cis*-products (XXIV).

Experimental

M. p.s were observed on a microscope hot stage. Ultraviolet light absorption measurements were made in 96% ethanol. Light petroleum refers to the fraction of boiling range 40—60°, unless otherwise stated. Chromatographic alumina was Type H from Messrs. Peter Spence & Sons, Ltd., unless otherwise stated.

Stereoisomerisation of cis-syn-1 : 2 : 3 : 4 : 5 : 6 : 12 : 13 : 14 : 15-*Decahydro*-8-*methoxy*-1 : 4-*dioxochrysene* (I) *by Alkaline Alumina.—The preparation of* trans-anti- (II) *and* (?)trans-syn-1 : 2 : 3 : 4 : 5 : 6 : 12 : 13 : 14 : 15-*Decahydro*-8-*methoxy*-1 : 4-*dioxochrysene* (V). A solution of the *cis-syn*-diketone (I) (4·0 g.) in benzene (1 l.) was allowed to percolate slowly down a column (internal diam., 4·5 cm.) of alkaline alumina (150 g.); the benzene effluent left no residue on evaporation. Elution with benzene–chloroform (1 : 1) (1·5 l.) gave a pale yellow effluent (A)

[6] Cf. styrylacetic acid (100%) ⇢ ⇠ γ-phenylcrotonic acid (0%), Bougault, *Compt. rend.*, 1917, **164**, 635; Ingold, "Structure and Mechanism in Organic Chemistry," G. Bell & Sons, Ltd., London, 1953, p. 563.

[7] Wieland and Stenzl, *Ber.*, 1907, **40**, 4825.

[8] Zimmerman, *J. Org. Chem.*, 1955, **20**, 549; Zimmerman and Giallombardo, *J. Amer. Chem. Soc.*, 1956, **78**, 6259.

followed by a brown effluent (B), which was collected separately. Evaporation of the two effluents and crystallisation of the residue from benzene–light petroleum gave trans-anti-1 : 2 : 3 : 4 : 5 : 6 : 12 : 13 : 14 : 15-*decahydro*-8-*methoxy*-1 : 4-*dioxochrysene* (II) as stout colourless needles (2·42 g.), m. p. 172—174° (Found: C, 76·9; H, 6·9. $C_{19}H_{20}O_3$ requires C, 77·0; H, 6·8%), $\lambda_{max.}$ 262 and 294 mμ (log ε 4·28 and 3·50).

Concentration of the mother-liquors from fraction (A) afforded a mixture of stout needles and rosettes of fine needles which were separated by hand-sorting. Several recrystallisations of the latter from benzene–light petroleum gave the (?)trans-syn-*stereoisomer* (V) as fine needles (0·20 g.), m. p. 174—176°, strongly depressed on admixture with the *trans-anti*-stereoisomer (Found: C, 76·8; H, 6·6%); $\lambda_{max.}$ 262 and 295 mμ (log ε 4·28 and 3·50). The mother-liquors from fraction (B) contained tar which interfered with attempts to isolate the minor component.

Effect of Hydrochloric Acid and Alcohols on trans-anti-1 : 2 : 3 : 4 : 5 : 6 : 12 : 13 : 14 : 15-*Decahydro*-8-*methoxy*-1 : 4-*dioxochrysene* (II).—(a) *Hydrochloric acid and methanol.* The *trans-anti*-diketone (II) (0·5 g.), suspended in boiling methanol (20 c.c.), was treated with concentrated hydrochloric acid (1 c.c.) and heated under reflux for 30 min. After 7 min. a clear yellow solution was obtained. The product (0·48 g.) was recovered crystalline by addition of water, and fractional crystallisation from ethanol afforded *cis*-1 : 2 : 3 : 4 : 5 : 6 : 11 : 12 : 13 : 14-decahydro-8-methoxy-1 : 4-dioxochrysene (VI) (0·22 g.), m. p. 153—156°, and 5 : 6 : 11 : 12-tetrahydro-1 : 8-dimethoxychrysene (VII; R = Me) (0·15 g.), m. p. 125—127°, identical with specimens obtained previously.[1,4]

(b) *Hydrochloric acid and ethanol.* A similar experiment on a smaller scale employing ethanol and concentrated hydrochloric acid gave as main product 1-ethoxy-5 : 6 : 11 : 12-tetrahydro-8-methoxychrysene (VII; R = Et), m. p. 119—120°, identical with a specimen obtained previously.[1,4]

(c) *Hydrochloric acid and propan-1-ol.* Under similar conditions propan-1-ol afforded 5 : 6 : 11 : 12-*tetrahydro*-8-*methoxy*-1-n-*propoxychrysene* (VII; R = Pr^n) which crystallised from propan-1-ol in laths, m. p. 82—82·5° (Found: C, 82·3; H, 7·7. $C_{22}H_{24}O_2$ requires C, 82·5; H, 7·6%), $\lambda_{max.}$ 218, 317, 330, and 346 mμ (log ε 4·28, 4·43, 4·50, and 4·35 respectively).

Effect of Methanolic Hydrogen Chloride on trans-anti-1 : 2 : 3 : 4 : 5 : 6 : 12 : 13 : 14 : 15-*Decahydro*-8-*methoxy*-1 : 4-*dioxochrysene* (II).—The *trans-anti*-diketone (II) (0·2 g.), suspended in boiling methanol (10 c.c.), was treated with saturated methanolic hydrogen chloride (3 drops) and kept at the b. p. for 10 min. On cooling, *cis*-1 : 2 : 3 : 4 : 5 : 6 : 11 : 12 : 13 : 14-decahydro-1 : 1 : 8-trimethoxy-4-oxochrysene (VIII) (0·13 g.), m. p. 135—138°, separated, identical with a specimen obtained previously.[4]

Effect of Hydrochloric Acid and Methanol on (?)-trans-syn-1 : 2 : 3 : 4 : 5 : 6 : 12 : 13 : 14 : 15-*Decahydro*-8-*methoxy*-1 : 4-*dioxochrysene* (V).—In a similar manner the (?)*trans-syn*-diketone (V) (0·2 g.) in boiling methanol was treated with concentrated hydrochloric acid (1 c.c.) and heated under reflux for 30 min. The product was separated into 5 : 6 : 11 : 12-tetrahydro-1 : 8-dimethoxychrysene (VII; R = Me), m. p. 124—126°, and *cis*-1 : 2 : 3 : 4 : 5 : 6 : 11 : 12 : 13 : 14-decahydro-8-methoxy-1 : 4-dioxochrysene (VI). The latter was obtained as laths, m. p. 148·5—150°, a new crystalline modification, which was interconvertible with the form previously encountered (plates, m. p. 154—157°); the infrared spectra of the two crystalline forms were almost identical (KCl discs).

Catalytic Hydrogenation of trans-anti-1 : 2 : 3 : 4 : 5 : 6 : 12 : 13 : 14 : 15-*Decahydro*-8-*methoxy*-1 : 4-*dioxochrysene* (II).—The *trans-anti*-diketone (II) (0·1 g.) in ethyl acetate (25 c.c.) was shaken in hydrogen at atmospheric pressure and room temperature in the presence of 2% palladised strontium carbonate (0·1 g.). Absorption of 1 mol. of hydrogen was complete in 2 hr. After recovery in the usual way, recrystallisation of the solid residue from aqueous ethanol afforded trans-anti-cis-1 : 2 : 3 : 4 : 5 : 6 : 11 : 12 : 13 : 14 : 15 : 16-*dodecahydro*-8-*methoxy*-1 : 4-*dioxochrysene* (III) as fine needles (50 mg.), m. p. 171—174° (Found: C, 76·3; H, 7·5. $C_{19}H_{22}O_3$ requires C, 76·5; H, 7·4%), $\lambda_{max.}$ 222 (infl.) and 280 mμ (log ε 3·88 and 3·34). The stereochemical configuration was confirmed by an experiment described below and by the instability of the compound to passage in solution down a column of alkaline alumina.

On a larger scale, with ethanol (100 c.c.) as solvent for the *trans-anti*-diketone (II) (1·0 g.), a crystalline precipitate separated after the absorption of slightly more than 1 mol. of hydrogen, and hydrogenation then ceased. Filtration afforded the *trans-anti-cis*-dodecahydro-diketone (III) described above. The material recovered from the filtrate was dissolved in ethyl acetate

XUM

(100 c.c.) and hydrogenation was continued in the presence of Adams's platinum oxide catalyst (0·1 g.) until no further absorption took place (total, 2·5 mol.). The residue, left on removal of the catalyst and evaporation of the solvent, was chromatographed on activated alumina (30 g.; Messrs. Savory and Moore Ltd., chromatographic analysis grade). Two main fractions were obtained on elution with benzene and benzene–chloroform (9 : 1) respectively. The first fraction (0·29 g.) on crystallisation from ethyl acetate–light petroleum afforded a *hydroxy-ketone* in the form of plates, m. p. 181—185° (Found: C, 76·2; H, 8·0. $C_{19}H_{24}O_3$ requires C, 76·0; H, 8·1%), $\lambda_{max.}$ 279 mμ (log ε 3·34). The second fraction (0·10 g.) on recrystallisation gave a second *hydroxy-ketone* as needles, m. p. 171—172·5° (Found: C, 76·0; H, 8·1%), having an infrared absorption spectrum markedly different from that of the isomeric substance of m. p. 181—185°. Oxidation of the hydroxy-ketone, m. p. 171—172·5° (60 mg.), in acetic acid (5 c.c.) with chromium trioxide (56 mg., 3 equiv.) at room temperature overnight followed by isolation of the product in chloroform afforded the corresponding *diketone*, crystallising from ethanol in laths, m. p. 181—184° (Found: C, 76·3; H, 7·5. $C_{19}H_{22}O_3$ requires C, 76·5; H, 7·4%). The infrared spectrum of this diketone differed markedly from that of the *trans-anti-cis*-diketone (III), m. p. 171—174°, described above, and, on analogy with experience in the perhydrophenanthrene series,[3] the diketone, m. p. 181—184°, was doubtless *trans-anti-trans*-1 : 2 : 3 : 4 : 5 : 6 : 11 : 12 : 13 : 14 : 15 : 16-dodecahydro-8-methoxy-1 : 4-dioxochrysene (IV).

The hydroxy-ketone, m. p. 171—172·5°, was recovered unchanged after 1·5 hours' heating under reflux with 5% methanolic potassium hydroxide. On treatment with excess of toluene-*p*-sulphonyl chloride in pyridine at room temperature it afforded a *toluene*-p-*sulphonate*, fine needles (from ethyl acetate–light petroleum), m. p. 174—176° (Found: C, 68·3; H, 6·9. $C_{26}H_{30}O_5S$ requires C, 68·7; H, 6·7%).

Catalytic Hydrogenation of cis-syn-1 : 2 : 3 : 4 : 5 : 6 : 12 : 13 : 14 : 15-*Decahydro*-1 : 1 : 8-*trimethoxy*-4-*oxochrysene* (IX) *and Transformations of the Products Therefrom.* trans-anti-cis-1 : 2 : 3 : 4 : 5 : 6 : 11 : 12 : 13 : 14 : 15 : 16-*Dodecahydro*-8-*methoxy*-1 : 4-*dioxochrysene* (III).—(*a*) Pure trimethoxy-ketone (IX) (0·34 g.) in ethyl acetate (25 c.c.) was hydrogenated at room temperature and atmospheric pressure in presence of Adams's platinum oxide catalyst (50 mg.). Absorption of hydrogen ceased after less than one-third of the calculated requirement, and ultraviolet spectrophotometry indicated that double-bond migration had taken place to the extent of 84% ($\lambda_{max.}$ 274 mμ; log ε 4·13, calc. on *M* 342). Removal of the catalyst and evaporation of the solvent gave a residue, which, on crystallisation from methanol, afforded *cis*-1 : 2 : 3 : 4 : 5 : 6 : 11 : 12 : 13 : 14-decahydro-1 : 1 : 8-trimethoxy-4-oxochrysene [4] (VIII), m. p. and mixed m. p. 135—137°.

(*b*) Pure trimethoxy-ketone (IX) (0·5 g.), suspended in methanol (50 c.c.), was hydrogenated at room temperature and atmospheric pressure in the presence of 10% palladised strontium carbonate (1·0 g.). Rapid absorption of the theoretical volume of hydrogen occurred, and filtration of the catalyst and evaporation of the solvent under reduced pressure with the minimum application of heat gave a gum which failed to crystallise ($\lambda_{max.}$ 278 mμ; log ε 3·38, calc. on *M* 344). On prolonged storage in contact with methanol the gum formed massive prisms which proved to be *cis-syn-cis*-1 : 2 : 3 : 4 : 5 : 6 : 11 : 12 : 13 : 14 : 15 : 16-dodecahydro-8-methoxy-1 : 4-dioxochrysene [1] (X), m. p. and mixed m. p. 161—165°.

(*c*) The trimethoxy-ketone (IX) (0·33 g.) in methanol (40 c.c.) was hydrogenated as in (*b*) (above). After removal of the catalyst, potassium hydroxide (0·4 g.) in a few drops of water was added, and the mixture was heated under reflux for 1 hr., cooled, and poured into water containing a slight excess of acetic acid. The product was extracted with chloroform (five times), and the combined extracts were washed successively with water, aqueous sodium hydrogen carbonate solution, and water, then dried and evaporated under reduced pressure with the minimum application of heat, to give a brown gum. On dissolution of this in a small volume of warm acetic acid and addition of water a solid separated. Crystallisation from methanol–ethyl acetate then afforded *trans-anti-cis*-1 : 2 : 3 : 4 : 5 : 6 : 11 : 12 : 13 : 14 : 15 : 16-dodecahydro-8-methoxy-1 : 4-dioxochrysene (III), m. p. 169—173°, identical in m. p., mixed m. p., and infrared absorption spectrum with the specimen obtained as above by catalytic hydrogenation of *trans-anti*-1 : 2 : 3 : 4 : 5 : 6 : 12 : 13 : 14 : 15-decahydro-8-methoxy-1 : 4-dioxochrysene (II).

Alkaline Equilibration of cis-syn-1 : 2 : 3 : 4 : 5 : 6 : 12 : 13 : 14 : 15-*Decahydro*-1 : 1 : 8-*trimethoxy*-4-*oxochrysene* (IX).—Freshly purified ketal (IX) (0·50 g.; $\lambda_{max.}$ 265·5 and 300·5 mμ; log ε 4·29 and 3·56) in methanol (50 c.c.) containing potassium hydroxide (2·5 g.) was heated

under reflux for 1 hr. After rapid cooling, water was added to cloudiness; when crystallisation was complete the solid was collected and dried in air [0·47 g.; m. p. 130—150°; $\lambda_{max.}$ 264 and 293—298 (plateau) mμ; log ε 4·31 and 3·56]. Repeated crystallisation from methanol of a portion of the solid gave only a small recovery of starting material, and the other component of the mixture could not be isolated.

A portion of the crude product (0·20 g.) was dissolved by gentle warming in acetic acid (2 c.c.), and water was added after a few minutes. The precipitated yellowish needles (0·14 g.) had m. p. 155—185°, and were separated by repeated crystallisation from methanol into a less soluble fraction (23 mg.), fine needles, m. p. 200—203°, identical with the *cis-syn*-diketone (I), and a more soluble fraction (32 mg.), stout needles, m. p. 175—177°, identical with the *trans-anti*-stereoisomer (II), described above.

Reduction of cis-syn-1 : 2 : 3 : 4 : 5 : 6 : 12 : 13 : 14 : 15-*Decahydro*-1 : 1 : 8-*trimethoxy*-4-*oxochrysene* (IX) *by Lithium Aluminium Hydride.* cis-syn-1 : 2 : 3 : 4 : 5 : 6 : 12 : 13 : 14 : 15-*Decahydro*-4-*hydroxy*-1 : 1 : 8-*trimethoxychrysene* (XIII).—Pure trimethoxy-ketone (IX) [2] (0·5 g.) in dry ether (200 c.c.) was added slowly to a stirred suspension of lithium aluminium hydride (0·5 g.) in ether (100 c.c.) at 0° during 1 hr. After a further ½ hr. the excess of reagent was decomposed by a little saturated aqueous sodium sulphate solution, followed by anhydrous sodium sulphate. The ethereal solution was decanted and evaporated after the addition of a drop of pyridine. Crystallisation of the solid residue from light petroleum (b. p. 60—80°) afforded cis-syn-1 : 2 : 3 : 4 : 5 : 6 : 12 : 13 : 14 : 15-*decahydro*-4-*hydroxy*-1 : 1 : 8-*trimethoxychrysene* (XIII) as needles, m. p. 146—150° (Found: C, 73·5; H, 8·1. $C_{21}H_{28}O_4$ requires C, 73·2; H, 8·2%), $\lambda_{max.}$ 266 and 300 mμ (log ε 4·32 and 3·59 respectively). The compound (XIII) failed to form a toluene-*p*-sulphonate on treatment at room temperature with an excess of toluene-*p*-sulphonyl chloride in pyridine. On dissolution of the substance (XIII) in warm acetic acid, stout needles separated, and recrystallisation from ethyl acetate afforded *cis-syn*-1 : 2 : 3 : 4 : 5 : 6 : 12 : 13 : 14 : 15-decahydro-4-hydroxy-8-methoxy-1-oxochrysene [1] (XIV), m. p. and mixed m. p. 189—192°.

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43. *Interaction of Lewis Acids with Aromatic Hydrocarbons and Bases. Part XVIII.* Aromatic Hydrocarbon Picrates in Chloroform.*

By R. Foster, D. Ll. Hammick, and S. F. Pearce.

Stability constants of fourteen hydrocarbon picrates in chloroform solution have been determined by a partition method. The stabilities have been related to the frequencies of the charge-transfer bands of the molecular complexes of the same hydrocarbons with chloranil.

Mulliken [1] has described the ground state of an intermolecular charge-transfer complex as ψ_N where:

$$\psi_N = x\psi(a,b) + y\psi(a^- - b^+) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

a and b represent the electron acceptor and the electron donor respectively, $\psi(a,b)$ is a no-bond function and $\psi(a^- - b^+)$ is a dative function in which an electron has been donated from b to a. An excited state ψ_E exists where:

$$\psi_E = x\psi(a^- - b^+) - y\psi(a,b) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

The energy of the excitation $\psi_N \longrightarrow \psi_E$ can be expressed approximately as: [2]

$$h\nu_{CT} = I_p - E - W \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

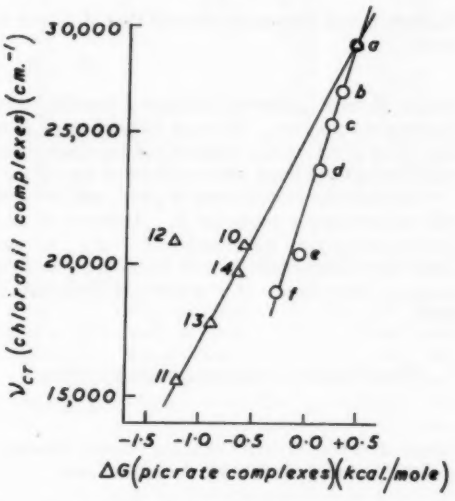
where ν_{CT} is the frequency of the charge-transfer absorption band, I_p is the ionisation

* Part XVII, *J.*, 1956, 3881.

[1] Mulliken, *J. Amer. Chem. Soc.*, 1952, **74**, 811; *J. Phys. Chem.*, 1952, **56**, 801.

potential of b, E is the electron affinity of a, and W is the dissociation energy of the charge-transfer excited state. If W can be taken as approximately constant for a series of complexes with the same acceptor molecule, then ν_{CT} is proportional to I_p.

In the ground state of the molecule (eqn. 1) normally $x \gg y$. Nevertheless the free energies of formation (ΔG) of the complexes between a series of donors and a particular acceptor are generally proportional to the corresponding I_p values provided that the donors are of the same type and there are no excessive steric factors.[2,3,4,5] Combination of these two relationships leads to the expectation of a proportionality between the corresponding



Plot of the free energies of formation of hydrocarbon picrate complexes against the frequencies of the charge-transfer bands of the corresponding hydrocarbon complexes with chloranil.

a Benzene, *b* toluene, *c* *m*-xylene, *d* mesitylene, *e* durene, *f* hexamethylbenzene. The numbers refer to the hydrocarbons given in the Table.

values of ΔG and ν_{CT} for such a series of complexes.[3] Likewise there should be a linear relationship between ν_{CT} for a series of donors with a particular acceptor against ν_{CT} for complexes of the same series of donors with a second acceptor. This has also been verified.[6] Hence we should expect a linear relationship between ν_{CT} for complexes of a series of donors with a given acceptor and ΔG for complexes of the same series of donors with a second acceptor—provided that the donors have the same type of structure and that no excessive steric effects are involved. This we find to be approximately the case.

Details of the experimental determination of ΔG by a partition method are now given for a series of hydrocarbon picrates. For the series involving the planar condensed aromatic donors benzene, naphthalene, anthracene, phenanthrene, acenaphthene, and fluorene values of ΔG for the picrate complexes are compared with the values of ν_{CT} for the corresponding chloranil complexes (Figure). On the Figure are also plotted points for complexes involving methylbenzenes, for which values of ΔG have been calculated from the stability constants quoted by Anderson and Hammick.[7] There is good agreement except for phenanthrene. Here the stability of the picrate is comparable with that of anthracene, as might be expected, but ν_{CT} for the chloranil complex is relatively high. Nevertheless this value of ν_{CT} might be expected from the ionisation potential of phenanthrene as calculated by Pople.[8]

[2] McConnell, Ham, and Flatt, *J. Chem. Phys.*, 1953, **21**, 66.
[3] Foster, Hammick, and Parsons, *J.*, 1956, 555.
[4] Briegleb and Czekalla, *Z. Electrochem.*, 1955, **59**, 184.
[5] Keefer and Andrews, *J. Amer. Chem. Soc.*, 1955, **77**, 2164.
[6] Foster, *Nature*, 1958, **181**, 337.
[7] Anderson and Hammick, *J.*, 1950, 1089.
[8] Pople, *J. Phys. Chem.*, 1957, **61**, 1.

Experimental

The stabilities of the picrates in chloroform at 18° were measured by Anderson and Hammick's [7] partition method. This, a modification of that described by Moore, Shepherd, and Goodall,[9] depends on the change in the partition of picric acid between water and chloroform when an aromatic hydrocarbon is added to the system. Allowance is made for the depressive effect of the hydrocarbon on the solubility of picric acid in the chloroform. The association of the hydrocarbon with the picric acid is expressed as:

$$K = [\text{complex}]/[\text{hydrocarbon}][\text{picric acid}] \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

Anderson and Hammick showed that if K and the effect of the solubility depression are small, then:

$$K = K_1 + k \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

where K_1 is a parameter obtained directly from the experimental data, and k is a solubility depression constant. Because the values of K measured in the present work are in some cases four to five times the highest values obtained by Anderson and Hammick,[7] a more accurate relationship has been used in place of eqn. (5).

Consider the distribution of picric acid between water and chloroform, in the latter of which the solution has a molarity P. Addition of an aromatic substance depresses the molarity of picric acid to y by the amount $(P - y)$. At the same time the total molarity of picric acid (free and complexed) in the chloroform is increased to y_1 by the amount $(y_1 - P)$ owing to complex formation. If Y is the experimentally found molarity of picric acid in the chloroform, then

$$Y = y + y_1 - P \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

The solubility depression constant being:

$$k = (P - y)/yZ \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

where Z is the molarity of the aromatic substance in the chloroform layer and P is the initial molarity of the picric acid, then from eqn. (7):

$$y = P/(1 + kZ) \simeq P(1 - kZ + k^2Z^2)$$

Substitution of this value of y in eqn. (6) gives:

$$y_1 - P = Y - P + PkZ - Pk^2Z^2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (8)$$

The stability constant

$$K = \frac{y_1 - P}{P[Z - (y_1 - P)]} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (9)$$

whence, since $(y_1 - P)$ is small compared with Z:

$$K = (y_1 - P)/[PZ(1 - KP)] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (10)$$

Eliminating y_1 from eqns. (8) and (10) we have:

$$K(1 - KP) = (Y - P)/PZ + k - k^2Z \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (11)$$

or

$$K = (K_1 + k - k^2Z)/(1 - KP) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (12)$$

where $K_1 = (Y - P)/PZ$ (the "apparent" stability constant). Anderson and Hammick showed that $k = 0{\cdot}0038V$ where V is the molecular volume of the hydrocarbon. This relationship has been used to determine k and hence K by eqn. (12). The molecular volumes determined by Tyrer [10] do not vary greatly for small changes in temperature or for certain solvent changes. The values used, obtained from standard data, are quoted in the Table.

The absorption maxima of the chloranil complexes were obtained from the spectra of chloroform solutions in which the concentration of chloranil $\approx 10^{-3}$M and the concentration of the hydrocarbon $\approx 10^{-1}$M. In all the cases the maxima were observed in the mixtures. No attempt was made to resolve the absorption bands of the various species present.

[9] Moore, Shepherd, and Goodall, *J.*, 1931, 1447.
[10] Tyrer, *J.*, 1910, **97**, 2620.

TABLE.

Hydrocarbon	Molecular volume V (ml.)	Solv.	Temp.	Ref.	K_1 (l./mole)	K	ΔG (kcal./mole)
1. Diphenyl	148	$CHCl_3$	25°	(*a*)	0·41	0·97	0·02
2. Diphenylmethane	167	C_6H_6	25	(*b*)	0·09	0·66	0·24
3. Triphenylmethane	226	$CHCl_3$	25	(*a*)	−0·27	0·52	0·38
4. Dibenzyl	183	—	—	(*c*)	0·08	0·70	0·21
5. Stilbene	174	C_6H_6	18	(*d*)	1·10	1·80	−0·34
6. Tolan	179	C_6H_6	18	(*d*)	0·83	1·54	−0·25
7. Tetraphenylethane	302	C_6H_6	25	(*e*)	−0·24	0·83	0·11
8. Tetraphenylethylene	298	C_6H_6	25	(*e*)	−0·63	0·22	0·87
9. Diphenyldiacetylene	200	C_6H_6	25	(*e*)	0·51	1·22	−0·11
10. Naphthalene	123	$CHCl_3$	18	(*f*)	2·03	2·68	−0·57
11. Anthracene	201	C_6H_6	20	(*g*)	5·00	7·56	−1·17
12. Phenanthrene	157	$C_6H_5{\cdot}CH_3$	20	(*a*)	5·41	8·04	−1·20
13. Acenaphthene	142	$CHCl_3$	25	(*a*)	3·46	4·36	−0·85
14. Fluorene	152	C_6H_6	25	(*e*)	2·09	2·87	−0·61

[a] Tyrer, *J.*, 1910, **97**, 2620. [b] Hampson, Farmer, and Sutton, *Proc. Roy. Soc.*, 1934, *A*, **143**, 147. [c] Computed from molecular volume of diphenylmethane by adding 16 ml. for the extra methylene group; Cohn, McMeekin, Edsall, and Blanchard, *J. Amer. Chem. Soc.*, 1934, **56**, 784. [d] Smythe and Dornte, *ibid.*, 1931, **53**, 1296. [e] Present work. [f] Forch, *Ann. Physik*, 1905, **17**, 1012. [g] Tyrer, *J.*, 1910, **97**, 1778.

Analytical Methods and Apparatus.—These are as described by Anderson and Hammick.[7] Spectra were measured on a Unicam S.P. 500 Spectrophotometer.

Materials.—Picric acid, recrystallised once from very dilute sulphuric acid, then four times distilled water and dried (P_2O_5), had m. p. 122·5°. Chloranil, recrystallised four times from benzene, had m. p. 289° (sealed tube). Chloroform was washed five times with water, four times with concentrated sulphuric acid, once with 5% sodium hydroxide solution, and finally thrice with ice-cold water, care being taken to avoid direct light, dried ($CaCl_2$), refluxed, and fractionated over P_2O_5 and stored away from the light in dark bottles completely filled. Hydrocarbons were prepared and purified by standard methods.

Results.—These are summarised in the Table. To illustrate the method of computation a single example is quoted in full, *viz.*, the stability constant K for anthracene picrate in chloroform at 18°:

Concentration of thiosulphate = 0·03372 mole/kg.; concentration of anthracene in the chloroform layer Z = 0·05209M; concentration of picric acid in the chloroform layer: three titrations gave:

Density of chloroform layer	1·4912	1·4912	1·4914 g./ml.
Wt. of $Na_2S_2O_3$ soln./wt. of $CHCl_3$ layer	0·8021	0·8029	0·8030

Average density = 1·492 g./ml. Average ratio = 0·8027. Hence concentration of picric acid in the chloroform layer, Y = (1·492 × 0·8027 × 0·03372) = 0·04036M. Concentration of picric acid in the water layer: two determinations gave:

Density of water layer	1·004	1·0046 g./ml.
Wt. of $Na_2S_2O_3$ soln./wt. of water layer	0·7121	0·7136

Average density = 1·0045 g./ml. Average ratio = 0·7128. Hence concentration of picric acid in the water layer, X = (1·0045 × 0·7128 × 0·03372) = 0·02414M.

From a graphical interpolation of the partition coefficient of picric acid between water and chloroform, the concentration P of picric acid in pure chloroform corresponding to a concentration 0·0241M in water is 0·03201M, whence the apparent stability constant:

$$K_1 = (Y - P)/PZ = 0{\cdot}00835/(0{\cdot}03201 \times 0{\cdot}05209) = 5{\cdot}00 \text{ l./mole.}$$

The molecular volume of anthracene in benzene at 20° is 201 ml.,[11] whence K = (201 × 0·0038) = 0·76 l./mole, and from (12) $K = 5{\cdot}73/(1 - 0{\cdot}032K)$, whence K = 7·56 l. mole.

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[11] Tyrer, *J.*, 1910, **97**, 1778.

44. *Reactions of* 1 : 2-*Dichloro*-3 : 4-*epoxybutane and Related Compounds.*

By E. G. E. Hawkins.

1 : 2-Dichloro-3 : 4-epoxybutane has been prepared as a mixture of isomers by oxidation of 3 : 4-dichlorobut-1-ene with performic acid. Hydration of the epoxide isomers leads to corresponding isomeric glycols and 4-chlorotetrahydrofuran-3-ols; the reactions of these compounds with alkali have been studied. The epoxides have been dehydrochlorinated to 2-chloro-3 : 4-epoxybut-1-ene and converted into isomeric 1 : 3 : 4-trichlorobutan-2-ols by hydrogen chloride.

Oxidation of 3 : 4-dichlorobut-1-ene to 1 : 2-dichloro-3 : 4-epoxybutane by peracetic acid has been recently described in a patent,[1] but the use of performic acid has been reported to give the corresponding glycol [2] in rather poor yield. It has now been found, however, that by limiting the reaction time and using $\frac{1}{4}$—$\frac{1}{2}$ molar quantities of formic acid the epoxide can be produced in reasonable yield.

However, although the glycol can be isolated (as a mixture of the two isomers) under Owen's conditions the yield depends on the time of heating of the crude product with water. Short heating leads to moderate yields of glycol, but longer heating gives almost completely a mixture of *cis*- and *trans*-4-chlorotetrahydrofuran-3-ols: 1 : 3 : 4-trichlorobutan-2-ol was also found in the product and evidently arose from reaction of the epoxide with hydrogen chloride produced by slow decomposition of the dichlorobutene. Further, the two isomeric glycols could be converted into the two chlorohydrins thermally (without solvent), by alcoholysis (with an acid catalyst), or by prolonged boiling with water. Only the *trans*-chlorohydrin (XV) has been previously reported [3] and its synthesis from 2 : 5-dihydrofuran has been repeated with hypochlorous acid replaced by *tert.*-butyl hypochlorite.

The epoxide prepared from 3 : 4-dichlorobut-1-ene and performic acid was found by vapour-phase chromatography to consist of two isomers (IX, XI), and concentrates of these isomers were obtained by fractional distillation. These two epoxides yielded the corresponding glycols (XII, XVI) and chlorotetrahydrofuranols (XIII, XV) on hydration.

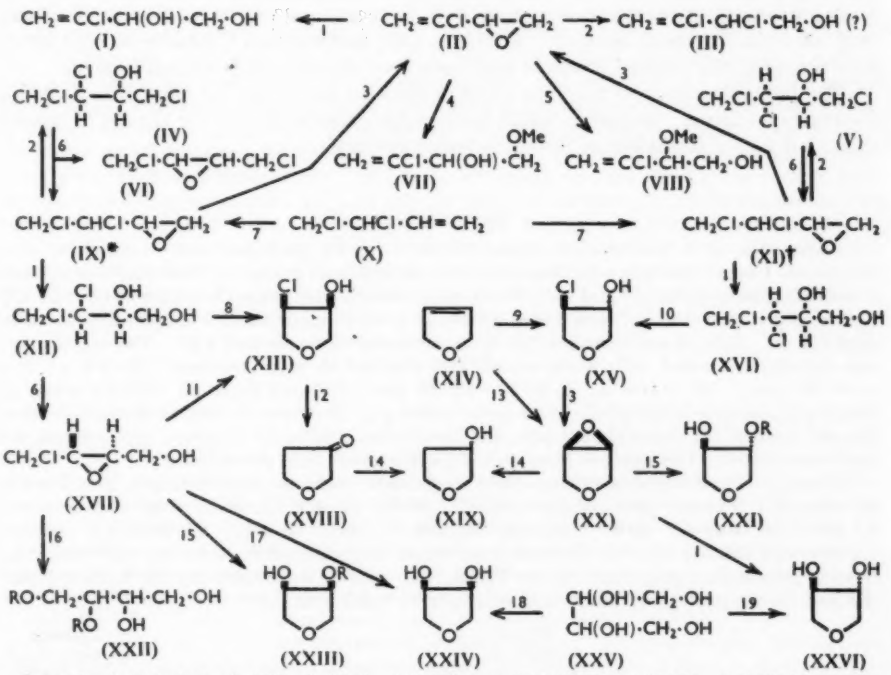
As reported by Reppe *et al.*[3], the *trans*-4-chlorotetrahydrofuran-3-ol (XV) gave 3 : 4-epoxytetrahydrofuran (XX) on alkali treatment; heating it with silver or cuprous oxide in a high-boiling inert solvent led to the same result. On the other hand, the *cis*-chlorohydrin (XIII) yielded red polymers on reaction with alkali, but heating it with cuprous or silver oxide in di*iso*propylbenzene gave, not an isomeric epoxide, but tetrahydrofuran-3-one (XVIII). Similar differences of behaviour between *cis*- and *trans*-halogenohydrins with alkali have been reported previously.[4] Both the epoxide (XX) and the ketone (XVIII), on catalytic reduction, gave tetrahydrofuran-3-ol (XIX).

The epoxytetrahydrofuran (XX), a water-soluble liquid, was synthesised, in poor yield, by reaction of peroxytrifluoroacetic acid with 2 : 5-dihydrofuran (XIV). Ring-opening of this epoxide with acid methanol provided *trans*-4-methoxytetrahydrofuran-3-ol (XXI; R = Me), and hydration yielded a *trans*-tetrahydrofuran-3 : 4-diol (XXVI) identical with that obtained by acid dehydration of dl-erythritol.

Reaction of either isomer of 1 : 2-dichloro-3 : 4-epoxybutane with alkali led to dehydrochlorination, with the formation of mainly 2-chloro-3 : 4-epoxybut-1-ene (II), identified by synthesis from chloroprene; [5] a by-product from this reaction, when sodium methoxide was used, was 1-chloro-2 : 3-epoxy-4-methoxybutane, formed through initial 1 : 2-epoxide

[1] Union Carbide Co., B.P. 784,620.
[2] Owen, *J.*, 1949, 241.
[3] Reppe, *et al.*, *Annalen*, 1955, **596**, 1.
[4] Bartlett, *J. Amer. Chem. Soc.*, 1935, **57**, 224.
[5] Cf. Petrov, *J. Gen. Chem., U.S.S.R.*, 1939, **9**, 2232; 1952, **22**, 1516.

ring opening to give 3 : 4-dichloro-1-methoxybutan-2-ol followed by ring closure by loss of hydrogen chloride from positions 2 and 3. The 2-chloro-3 : 4-epoxybut-1-ene (II) on hydration with aqueous acid gave the corresponding glycol (I). Opening of the epoxide ring with sodium methoxide yielded 3-chloro-1-methoxybut-3-en-2-ol (VII), but use of acid methanol led to reverse opening, to give 3-chloro-2-methoxybut-3-en-1-ol (VIII); these structures were confirmed by catalytic hydrogenation to the corresponding known methoxybutanols. Ring opening of the epoxy-butene (II) by ethereal hydrogen chloride or aqueous hydrochloric acid gave the same dichlorobutenol (III); Petrov [5] claimed that the primary alcohol is formed in such an addition, although the properties given for both the primary and the corresponding secondary alcohol appear to be very similar, and it seems possible that a mixture of the two is formed.



Reagents: 1, Hydration. 2, HCl. 3, Alkali. 4, NaOMe. 5, Acid–MeOH. 6, NaOH. 7 H·CO_2H. 8, Heat or alcoholysis. 9, Bu^{t}OCl. 10, Heat, alkali, or alcoholysis. 11, Heat. 12, Ag_2O. 13, CF_3·CO_2H. 14, H_2–Ni. 15, Acid–ROH. 16, NaOR. 17, Aq. H·CO_2H. 18, Dehydration(*meso*). 19, Dehydration (racemic).

* Low-boiling isomer. † High-boiling isomer.

Treatment of the isomeric 1 : 2-dichloro-3 : 4-epoxybutanes with hydrogen chloride produced two isomers (IV, V) of 1 : 3 : 4-trichlorobutan-2-ol, both of which were present in the reaction product of hydrogen chloride and 1 : 4-dichloro-2 : 3-epoxybutane. The *erythro*-trichlorobutanol (IV) with alkali gave, not only the lower-boiling epoxide isomer (IX) from which it came, but also 1 : 4-dichloro-2 : 3-epoxybutane (VI); the *threo*-trichlorobutanol (V) gave only its precursor (XI) under these conditions.

The two isomeric 3 : 4-dichlorobutane-1 : 2-diols behaved differently on reaction with alkali. The *threo*-isomer (XVI), m. p. 63—65°, derived from the higher-boiling epoxide (XI), when treated with 1 mol. of alkali lost hydrogen chloride from the 1 : 4-positions to give *trans*-4-chlorotetrahydrofuran-3-ol (XV), together with some epoxytetrahydrofuran (XX), whereas the *erythro*-isomer (XII), m. p. 69—70°, under similar conditions lost

hydrogen chloride from the 2 : 3-positions to yield mainly 4-chloro-2 : 3-epoxybutan-1-ol (XVII).

This chloroepoxybutanol was converted into the *cis*-chlorotetrahydrofuranol (XIII) by heat, and into *cis*-tetrahydrofuran-3 : 4-diol (XXIV) (identical with that from dehydration of *meso*-erythritol) by hydration. Reaction with alkanols, under acid-catalysed conditions, yielded *cis*-4-alkoxytetrahydrofuran-3-ols (XXIII), different from the corresponding *trans*-compounds (XXI) produced from epoxytetrahydrofuran under similar conditions. However, on further treatment with aqueous or alcoholic alkali or metal alkoxide, the chloroepoxybutanol was not converted into a tetrahydrofuran derivative by 1 : 4-ring closure but yielded an open-chain erythritol, or erythritol ether (XXII); aqueous sodium hydroxide gave *meso*-erythritol, methanolic sodium hydroxide yielded what was probably a methoxybutanetriol, and sodium methoxide provided a dimethoxybutanediol (probably mainly 3 : 4-dimethoxybutane-1 : 2-diol since analysis showed it to contain *ca.* 70% of vicinal hydroxy-groups). Although solid derivatives of these erythritol ethers were obtained, the original products may have been mixtures of positional isomers.

The probable nature of the stereoisomers involved in the present work is indicated in the reaction scheme; inversions would presumably occur at opening or closing of epoxide rings, but not at formation of tetrahydrofuran systems.

Experimental

Preparation of 1 : 2-*Dichloro*-3 : 4-*epoxybutane.*—(a) *By performic acid oxidation of* 3 : 4-*dichlorobut*-1-*ene.* The following was typical of experiments giving the best yields of epoxide. The dichlorobutene (500 g.) and 98% formic acid (140 g.) were stirred together at 60° and 85% hydrogen peroxide (185 c.c.) was added gradually so as to maintain the temperature at *ca.* 60° during 1 hr. Stirring was continued at this temperature for a further 4 hr. The organic layer was separated, washed with water, dried, and distilled to give fractions: (1) (8·1 g.) b. p. <39°/40 mm.; (2) (141·4 g.) b. p. 39—42°/40 mm.; (3) (8·1 g.) b. p. <65°/11 mm.; (4) (200·9 g.) b. p. 65—72°/11 mm.; and residue (138·8 g.). Fraction (2) was unchanged dichlorobutene, fraction (4) the crude epoxide, and the residue a mixture of glycol, glycol esters, and trichlorobutanol. The aqueous layer on distillation gave crude glycol (67 g.).

Crude *epoxide*, distilled at 100 mm. from magnesium oxide and under nitrogen, gave fractions as tabulated [Found: (low-boiling isomer) C, 34·05; H, 4·3; Cl, 50·3; (high-boiling isomer) C, 34·3; H, 4·4; Cl, 50·6. $C_4H_6OCl_2$ requires C, 34·0; H, 4·25; Cl, 50·35%]. Infrared spectroscopy showed that the fractions were free from unsaturation, hydroxyl, carbonyl, ether, or ester groups (except as noted in the Table). An epoxide equivalent (by the Nicolet–Poulter method) on a mixed isomer fraction gave a value of 143·3 (calc. 141).

			Epoxide isomers (%) *					Epoxide isomers (%) *	
B. p.	Wt. (g.)	n_D^{20}	low-boiling	high-boiling	B. p.	Wt. (g.)	n_D^{20}	low-boiling	high-boiling
100—110°	25·3	1·4758		†	114°	493·3	1·4740	85	15
110—112·5	21·5	1·4747	94	†	114—116	451·5	1·4746	70	30
112·5—113	7·9	1·4740	96	†	116—117	153·7	1·4768	10	90
113	30·8	1·4738	94	6	117—118·5	60·0	1·4767	5	95
113—114	30·8	1·4740	88	12	118·5—119	45·3	1·4758	<5	98

* By infrared spectroscopy or vapour-phase chromatography. † Contained dichlorobutene.

(b) Via *the bromohydrin.* *N*-Bromosuccinimide (76 g.) in water (320 c.c.) was stirred with 3 : 4-dichlorobut-1-ene (50 g.) in ether (320 c.c.) at room temperature until the solid had dissolved (2 days). The ethereal layer and extracts were combined, washed with sodium hydrogen carbonate solution, dried, and distilled, to give impure bromohydrin (43·8 g.), b. p. 60—67°/0·3 mm.; from the distillate a small quantity of 1 : 2-dibromo-3 : 4-dichlorobutane, m. p. 80—81°, separated.

The crude bromohydrin (38 g.) was suspended in water (20 c.c.) and vigorously stirred during the addition (10 min.) of sodium hydroxide (7·3 g.) in water (30 c.c.). Stirring was continued for a further 1½ hr., and the product worked up normally. There were obtained

impure epoxide (12·3 g.) and fractions (14·2 g.) containing tetrahalogenobutanes. Fractionation of the impure epoxide gave a distillate (11·0 g.), b. p. 175—177°, n_D^{20} 1·4810, shown by spectroscopy to be similar to, but slightly less pure than, that obtained by performic acid oxidation, and to consist almost completely of the low-boiling isomer.

Preparation of 3 : 4-*Dichlorobutane*-1 : 2-*diol.*—(a) *By performic acid oxidation of* 3 : 4-*dichlorobut*-1-*ene.* This was an unsatisfactory method, based on that described by Owen [2] who obtained only 2·0 g. of crude glycol from 12 g. of 3 : 4-dichlorobut-1-ene. From dichlorobutene (360 g.), 98—100% formic acid (740 c.c.), and 30% hydrogen peroxide (380 c.c.) at 45° during 21½ hr. were obtained unchanged olefin (160 g.) and fractions (i) (27·5 g.), b. p. <128°/15 mm., n_D^{20} 1·4865, (ii) (80·0 g.), b. p. 128—138°/15 mm., n_D^{20} 1·4900, (iii) (108·7 g.), b. p. 138—148°/15 mm., n_D^{20} 1·4911, and (iv) (12·8 g.), b. p. >148°/15 mm., n_D^{20} 1·4928. Some glycol was obtained by crystallisation of fractions (iii) and (iv) but the infrared spectra of the last three fractions showed that formates were still present. Further hydrolysis of the high-boiling fractions (186·8 g.) by boiling water (600 c.c.) for a further 1½ hr. gave fractions: (1) (16·7 g.), b. p. 88—95°/13 mm., n_D^{20} 1·4781, (2) (24·0 g.), b. p. 95—100°/13 mm., n_D^{20} 1·4845, (3) (65·1 g.), b. p. 100—106°/13 mm., n_D^{20} 1·4900, (4) (6·8 g.), b. p. 106—130°/13 mm., n_D^{20} 1·4943, and a residue (14·2 g.). These fractions were shown spectroscopically, and by the m. p.s and mixed m. p.s of their phenylurethanes, to consist of *cis*- and *trans*-4-chlorotetrahydrofuran-3-ols and 1 : 3 : 4-trichlorobutan-2-ol as obtained from alcoholysis of similar oxidation products (see p. 252). The extent of conversion of the glycol formate into the chlorotetrahydrofuranols was variable.

(b) *By hydration of the epoxides.* (i) The lower-boiling epoxide (20 g.) was heated, with shaking, with 1% aqueous sulphuric acid (50 c.c.) until the mixture became homogeneous, and then further epoxide (53·3 g.) added portionwise with heating and shaking until clear after each addition. The cooled solution was neutralised with solid sodium hydrogen carbonate, saturated with sodium chloride, and extracted with ethyl acetate. Evaporation of the solvent left crystalline *erythro*-3 : 4-dichlorobutane-1 : 2-diol (48·5 g.), which, after recrystallisation from carbon tetrachloride–ethyl acetate or carbon tetrachloride–chloroform, had m. p. 69·5—71° (Found: C, 29·9; H, 4·6; Cl, 44·8. Calc. for $C_4H_8O_2Cl_2$: C, 30·2; H, 5·0; Cl, 44·7%) [*bisphenylurethane*, m. p. 146—148° (Found: C, 54·35; H, 4·5; Cl, 17·8; N, 7·2. $C_{18}H_{18}O_4N_2Cl_2$ requires C, 54·4; H, 4·5; Cl, 17·9; N, 7·05%)].

(ii) The higher-boiling epoxide (5·7 g.) was treated as in (i) and yielded solid threo-*glycol* (4·5 g.), m. p. 63—65° (from carbon tetrachloride–chloroform) (Found: C, 30·35; H, 5·1; Cl, 44·8%) [*bisphenylurethane*, m. p. 170—172° (Found: C, 54·3; H, 4·4; Cl, 18·1; N, 7·2%)].

Preparation of Isomers of 4-*Chlorotetrahydrofuran*-3-*ol.*—(a) cis-*Chlorohydrin.* (i) *erythro*-3 : 4-Dichlorobutane-1 : 2-diol (10 g.) was heated under reflux for 2 hr. with water (50 c.c.), the water removed under reduced pressure, and the residue distilled to give fractions (1) (4·4 g.), b. p. 83—85°/11 mm., n_D^{20} 1·4880, and (2) (2·4 g.), b. p. 138—140°/11 mm., and a residue (0·8 g.). Fraction (2) and the residue were unchanged glycol which crystallised. Fraction (1) was *cis*-4-chlorotetrahydrofuran-3-ol [*phenylurethane*, m. p. 132—133° (Found: C, 54·7; H, 4·6; Cl, 14·9; N, 5·5. $C_{11}H_{12}O_3NCl$ requires C, 54·7; H, 5·0; Cl, 14·7; N, 5·8%)].

(ii) The *erythro*-glycol (3·0 g.) was heated at 180—200° for ½ hr. Hydrogen chloride was given off and the liquid darkened. Distillation gave the chlorohydrin (1·5 g.), b. p. 87—90°/15 mm., n_D^{20} 1·4891, identical spectroscopically with the product from (i).

(b) trans-*Chlorohydrin.* (i) *threo*-3 : 4-Dichlorobutane-1 : 2-diol (2·6 g.) was heated at 180—200° for ¾ hr., giving hydrogen chloride and darkening. Distillation gave *trans*-4-chlorotetrahydrofuran-3-ol (0·7 g.), b. p. 101—101·5°/14 mm., n_D^{20} 1·4796 [*phenylurethane*, m. p. 132—134° (Found: C, 54·9; H, 4·8; Cl, 14·65; N, 5·4%), depressed in m. p. on admixture with the phenylurethane of the *cis*-isomer]. The column drainings (0·8 g.) were found spectroscopically to consist of a mixture of the chlorohydrin and unchanged glycol.

(ii) Sodium hydroxide (5·0 g.) in water (6 c.c.) and methanol (18 c.c.) was added dropwise, during 10 min. at room temperature, to a stirred solution of the *threo*-glycol (20 g.) in methanol (20 c.c.). The mixture was heated for ½ hr. on the water-bath, cooled, filtered, and distilled. The distillate (5·8 g.), b. p. 102—104°/12—13 mm., n_D^{20} 1·4810 (Found: C, 39·8; H, 6·0; Cl, 28·75. Calc. for $C_4H_7O_2Cl$: C, 39·2; H, 5·7; Cl, 29·0%), gave the infrared spectrum and phenylurethane, m. p. and mixed m. p. 130—132°, of the *trans*-chlorohydrin. The residue (3·2 g.) was *erythro*-3 : 4-dichlorobutane-1 : 2-diol. The low recovery in this reaction was due to the formation of 3 : 4-epoxytetrahydrofuran, lost in the solvent removal, by further reaction of the chlorohydrin.

(iii) 2 : 5-Dihydrofuran (15·5 g.) was dissolved in acetic acid (70 g.) and water (5 g.), and *tert.*-butyl hypochlorite (30 g.) added with stirring and cooling during 2 hr. Then the mixture was heated at 40—45° for ½ hr., cooled, and extracted with ether. Distillation provided 3-acetoxy-4-chlorotetrahydrofuran (7·4 g.), b. p. 86—89°/11 mm., n_D^{20} 1·4577 (Found: C, 43·9; H, 5·7. Calc. for $C_6H_9O_3Cl$: C, 43·8; H, 5·5%). Alcoholysis with ethanol and toluene-*p*-sulphonic acid yielded the *trans*-chlorohydrin (3·2 g.), b. p. 100—102°/11—12 mm., n_D^{20} 1·4799 (Found: C, 39·4; H, 5·7; Cl, 29·1. Calc. for $C_4H_7O_2Cl$: C, 39·2; H, 5·7; Cl, 29·0%), identical with that above (infrared spectrum).

(c) *Mixed isomers.* 3 : 4-Dichlorobut-1-ene (360 g.) and 98% formic acid (1 l.) were stirred at 40° and 30% hydrogen peroxide (760 c.c.) was added gradually; stirring at this temperature was continued for *ca.* 20 hr. Water, formic acid, and unchanged dichlorobutene were then removed under reduced pressure and the residue was combined with that from a similar experiment. The combined products (248 g.) were heated under reflux with ethanol (400 c.c.) and toluene-*p*-sulphonic acid (2 g.) until production of ethyl formate (continuously taken off) was complete; the excess of ethanol was removed and the residue distilled to yield fractions (1) (161 g.), b. p. 40—120°/15 mm., and (2) (101·5 g.), b. p. 120—137°/13 mm. Fraction (2) provided crystalline glycol. Fraction (1) was acetylated with acetic anhydride, and the acetates were distilled to give fractions (i) (1·4 g.) b. p. 70—90°/12 mm., (ii) (142·0 g.) b. p. 90—96°/12 mm., n_D^{20} 1·4573, (iii) (6·6 g.) b. p. 96—115°/12 mm., and (iv) (24·8 g.) b. p. 115—138°/12 mm., n_D^{20} 1·4653, and residue (23·2 g.).

Fraction (ii) consisted of a mixture of the acetates of *cis*- and *trans*-4-chlorotetrahydrofuran-3-ol and hydrolysis, followed by fractionation of the product, gave the *cis*-isomer, b. p. 98—92°/12 mm., n_D^{20} 1·4883 (phenylurethane m. p. 132—133°), the *trans*-isómer, b. p. 99—103°/12 mm., n_D^{20} 1·4864 (phenylurethane m. p. 132—134°), and mixtures. These products were identical with those obtained from the corresponding isomeric glycols, above.

Fraction (iv), on redistillation, had b. p. 115—117°/12 mm., n_D^{20} 1·4752, and on alcoholysis yielded 1 : 3 : 4-trichlorobutan-2-ol, b. p. 105°/12 mm., n_D^{20} 1·5047 (Found: C, 27·25; H, 4·2; Cl, 59·3; OH, 9·6. Calc. for $C_4H_7OCl_3$: C, 27·0; H, 3·9; Cl, 60·0; OH, 9·6%) [*phenylurethane* m. p. 134—136° (Found: C, 44·6; H, 4·3; N, 4·8. $C_{11}H_{12}O_2NCl_3$ requires C, 44·5; H, 4·05; N, 4·7%)].

Reaction of Isomeric 4-Chlorotetrahydrofuran-3-ols with Bases.—(a) cis-*Isomer.* (i) The chlorohydrin (35·5 g.) was gradually added to fused potassium hydroxide at *ca.* 200° and the temperature raised to 250°. Liquid and gaseous products came off rapidly and the former were condensed, dried, and redistilled to give fractions: (1) (1·2 g.) b. p. 64—120°/760 mm., (2) (6·0 g.) b. p. 120—155° (mainly 135—138°)/760 mm., n_D^{20} 1·4432. Fraction (1) gave the 2 : 4-dinitrophenylhydrazone of tetrahydrofuran-3-one (see below); (2) consisted mainly of this ketone (infrared).

The residue in the reaction flask, when treated with water to remove inorganic compounds, left a red, chloroform-soluble polymer (10·5 g.). The aqueous extract also liberated acidic material (5·0 g.) on acidification, but this was not examined. The red polymer was found, from its infrared spectrum, to contain tetrahydrofuran rings, hydroxyl groups, and two carbonyl functions (alkyl ketone and tetrahydrofuranone type): these suggest self-condensation of tetrahydrofuranone with some ring-opening.

(ii) Treatment of the chlorohydrin with concentrated aqueous sodium hydroxide at room temperature gave a similar red polymer.

(iii) Di*iso*propylbenzene (30 g.) and a mixture (60 g.) of silver oxide and cuprous oxide were heated to 150° under a short, unpacked column, and the chlorohydrin (40 g.) added gradually as the product distilled off: the bath-temperature was raised to 220°. The wet distillate was dried and redistilled, to yield tetrahydrofuran-3-one (16·8 g.), b. p. 137—138°, n_D^{20} 1·4366 [2 : 4-dinitrophenylhydrazone, m. p. 159—161° (from ethanol) (Found: C, 45·2; H, 3·85; N, 20·85. Calc. for $C_{10}H_{10}O_5N_4$: C, 45·1; H, 3·8; N, 21·0%) (lit.,[6] m. p. 155°)].

The ketone (4 g.) in ethanol (5 c.c.) was hydrogenated at atmospheric pressure in the presence of Raney nickel (1 g.). Distillation of the products gave tetrahydrofuran-3-ol (3·0 g.), b. p. 177—179°, n_D^{20} 1·4481 [phenylurethane, m. p. and mixed m. p. 118·5—120·5° (Found: C, 64·0; H, 6·2; N, 6·75. Calc. for $C_{11}H_{13}O_3N$: C, 63·8; H, 6·3; N, 6·8%)].

(b) trans-*Isomer.* (i) The chlorohydrin (24 g.) was suspended in water (15 c.c.), and sodium hydroxide (8 g.) in water (15 c.c.) was added, with stirring, at room temperature. The exo-

[6] Yur'ev, Korobitsyna, and Savina, *Doklady Akad. Nauk S.S.S.R.*, 1952, **86**, 91.

thermic reaction caused the temperature to rise to 37°. The solution was saturated with sodium chloride and extracted three times with ether; the extracts yielded, on distillation, 3 : 4-epoxytetrahydrofuran (5·1 g.), b. p. 135—143°. Continuous extraction overnight of the aqueous phase with ether gave further epoxide (8·6 g.). The redistilled epoxide had b. p. 143—144°, n_D^{20} 1·4466 (Found: C, 56·5; H, 7·1. Calc. for $C_4H_6O_2$: C, 55·8; H, 7·0%), and its infrared spectrum showed it to contain a tetrahydrofuran ring but no carbonyl group. It gave an epoxide equivalent of *ca.* 85% of the calculated value by the Nicolet–Poulter method.

(ii) Cuprous oxide (10 g.) and di*iso*propylbenzene (10 g.) were heated together to *ca.* 150° and the chlorohydrin (10 g.) was added gradually. The product was taken off overhead from a heated, packed column, and the bath-temperature gradually raised to 220°. The wet product (7·6 g.) was dried and redistilled, to provide 3 : 4-epoxytetrahydrofuran (4·7 g.), b. p. 143—145°, n_D^{20} 1·4442.

The epoxide (6 g.) in ethanol (20 c.c.) was hydrogenated (Raney nickel) at 110°/150 atm. for 4 hr. Distillation of the product gave unchanged epoxide (2·0 g.) and tetrahydrofuran-3-ol (1·6 g.); the latter gave a phenylurethane, m. p. and mixed m. p. 119—120°.

(iii) 85% Hydrogen peroxide (12 g.) and methylene chloride (50 c.c.) were stirred and cooled in ice; trifluoroacetic anhydride (50·8 g.) was added in 15 min. The resulting solution was stirred for 10 min. in the cold, and then dropped, during ½ hr., into a stirred suspension of oven-dried sodium carbonate (95 g.) in methylene chloride (200 c.c.) containing 2 : 5-dihydrofuran (14 g.). The solvent gently boiled during the addition, and the mixture was heated for a further ½ hr. under reflux before filtration and washing of the separated solid with a little methylene chloride. Distillation of the dried methylene chloride solution gave a little unchanged dihydrofuran and 3 : 4-epoxytetrahydrofuran (1·0 g.), b. p. 130—140°, identical spectroscopically with the epoxide from (i) and (ii) above.

Reactions of 3 : 4-*Epoxytetrahydrofuran.*—(a) *Hydration.* The epoxide (5 g.) and water (5 g.) were heated together under reflux for 3 hr., the water and unchanged epoxide were removed and the residue was distilled, to give *trans*-tetrahydrofuran-3 : 4-diol (0·4 g.), b. p. 160—165°/15 mm., which although crystallising in the receiver was too hygroscopic for further purification. It provided a *bisphenylurethane*, m. p. 206—208° (Found: C, 63·0; H, 5·2; N, 8·3. $C_{18}H_{18}O_5N_2$ requires C, 63·2; H, 5·2; N, 8·2%).

Heating DL-erythritol [3] (16 g.) with phosphoric acid (0·4 g.) in a vacuum gave *trans*-tetrahydrofuran-3 : 4-diol (*ca.* 8 g.), b. p. 159—160°/13 mm., which yielded a bisphenylurethane, m. p. 207—208°, identical with that above.

(b) *Reaction with methanol.* The epoxide (6·5 g.) was added to boiling methanol (15 c.c.) containing a drop of sulphuric acid: heating was continued for 3½ hr. Addition of solid hydrogen carbonate, followed by filtration and distillation, gave a main fraction (3·7 g.), b. p. 103—104°/13 mm., n_D^{20} 1·4545, which showed in its infrared spectrum the presence of a tetrahydrofuran ring, an associated hydroxy- and a methoxy-group; it was *trans*-4-methoxytetrahydrofuran-3-ol [*phenylurethane*, m. p. 97—99° (from benzene–light petroleum) (Found: C, 61·2; H, 6·5; N, 6·0. $C_{12}H_{15}O_4N$ requires C, 60·8; H, 6·3; N, 5·9%).

Reaction of 1 : 2-*Dichloro*-3 : 4-*epoxybutane with Alkali.*—(i) 1 : 2-Dichloro-3 : 4-epoxybutane (low-boiling isomer; 22 g.) in methanol (11 c.c.) was treated with sodium hydroxide (6·4 g.) in water (8 c.c.) and methanol (22 c.c.) during ¾ hr. at room temperature with stirring. Stirring was continued until all the alkali had been consumed, and the product then diluted with water and extracted with ether. Distillation of the product gave fractions: (1) (2·6 g.) b. p. 102—109°/1 atm., n_D^{20} 1·4539; (2) (8·1 g.) b. p. 71—74°/15 mm., n_D^{20} 1·4553, and (3) (0·9 g.) b. p. 74—128°/15 mm., n_D^{20} 1·4592, and a residue (2·7 g.). Fraction 1 was unsaturated (infrared spectrum), but contained no OH, OMe or >CO group; it gave a low epoxide equivalent (85%) by the Nicolet–Poulter method. Redistillation gave 2-*chloro*-3 : 4-*epoxybut*-1-*ene*, b. p. 109—110·5°/1 atm., n_D^{20} 1·4570 (Found: C, 45·8; H, 5·6; Cl, 33·5. C_4H_5OCl requires C, 45·9; H, 4·8; Cl, 34·0%): it formed azeotropes with methanol or ethanol. Fraction 2 contained unsaturation, hydroxyl, and methoxyl functions; it reacted very slowly with α-naphthyl *iso*cyanate to give the *α-naphthylurethane*, m. p. 94—95°, of 3-chloro-1-methoxybut-3-en-2-ol (Found: C, 63·1; H, 5·1; Cl, 11·7; N, 4·7. $C_{16}H_{16}O_3NCl$ requires C, 62·8; H, 5·2; Cl, 11·6; N, 4·6%).

(ii) 1 : 2-Dichloro-3 : 4-epoxybutane (high-boiling isomer; 22 g.) in methanol (11 c.c.) was treated during 25 min., at *ca.* 60° with stirring, with sodium hydroxide (6·9 g.) in water (8 c.c.) and methanol (22 c.c.). Distillation of the product gave fractions: (1) (8·5 g.) b. p. 93—110°/1

atm., and (2) (5·0 g.) b. p. 65—73°/15 mm., n_D^{20} 1·4561, and a residue (1·7 g.). Fraction (1), after drying, was found to be identical with the unsaturated epoxide above, from the low-boiling dichloroepoxybutane, and fraction (2) was again 3-chloro-1-methoxybut-3-en-2-ol, yielding the above α-naphthylurethane.

(iii) 1 : 2-Dichloro-3 : 4-epoxybutane (mixed isomers; 100 g.) was dropped on molten potassium hydroxide (70 g.) at 150—160°, finally raised to 200°; the product flashed off into the receiver, and heating was continued until no more product distilled. Fractionation of the dried distillate gave the unsaturated epoxide and starting material; the latter was recycled, and there were finally obtained 2-chloro-3 : 4-epoxybut-1-ene (60·3 g.) and 1 : 2-dichloro-3 : 4-epoxybutane (3·3 g.).

(iv) Chloroprene (25 g.) in ether (250 c.c.) was stirred with *N*-bromosuccinimide (50 g.) in water (250 c.c.) at room temperature until all the solid had dissolved (3½ hr.); the reaction was slightly exothermic. The ether extracts on distillation yielded the bromohydrin (9·4 g.) of chloroprene; this had b. p. 78—85°/13 mm., n_D^{20} 1·5234 (Petrov [5] gives b. p. 77—77·25°/10 mm., n_D^{20} 1·5228); also formed were higher-boiling products, presumably tetrahalogenobutanols. The bromohydrin was converted into 2-chloro-3 : 4-epoxybut-1-ene (2·1 g.), b. p. 105—109°, n_D^{20} 1·4460, by Petrov's method; [5] its infrared spectrum was identical with that of material prepared from 1 : 2-dichloro-3 : 4-epoxybutane.

Reactions of 2-Chloro-3 : 4-epoxybut-1-ene.—(a) *Reaction with sodium methoxide.* (i) The chloroepoxybutene (3·0 g.), derived from the low-boiling dichloroepoxybutane, was heated under reflux for 2 hr. with methanol containing a little sodium methoxide. Distillation provided 3-chloro-1-methoxybut-3-en-2-ol, b. p. 71—72°/15 mm., n_D^{20} 1·4602, identical spectroscopically with that above.

(ii) The chloroepoxybutene from the high-boiling dichloroepoxybutane when treated as in (i) gave the same 3-chloro-1-methoxybut-3-en-2-ol (1·9 g.), b. p. 70—73°/13 mm., n_D^{20} 1·4601, as above (α-naphthylurethane, m. p. and mixed m. p. 94—95°).

Catalytic hydrogenation of the chloromethoxybutenol at atmospheric pressure was carried out with a Raney nickel catalyst and in the presence of aqueous-ethanolic sodium hydroxide (a slight excess over stoicheiometric based on the chlorine content); in 29½ hr. reaction was complete and yielded 1-methoxybutan-2-ol, b. p. 133—137°/1 atm., n_D^{20} 1·4114 [3 : 5-dinitrobenzoate, m. p. and mixed m. p. 92—94° (from methanol) (Found: C, 48·65; H, 4·9; N, 9·5. Calc. for $C_{12}H_{14}O_7N_2$: C, 48·3; H, 4·7; N, 9·4%)].

Similar hydrogenation of the crude chloromethoxybutenol fraction obtained by direct reaction of 1 : 2-dichloro-3 : 4-epoxybutane with sodium methoxide gave, in addition to 1-methoxybutan-2-ol, a fraction, b. p. 72—73°/14 mm., n_D^{20} 1·4436, identified as 1-chloro-2 : 3-epoxy-4-methoxybutane by comparison of its infrared spectrum with that of the synthetic compound.[7]

(b) *Reaction with acid methanol.* The chloroepoxybutene (15 g.) was heated under reflux for 2 hr. with methanol containing sulphuric acid (2 drops). The product was neutralised, filtered, and distilled, to give 3-chloro-2-methoxybut-3-en-1-ol (16·2 g.), b. p. 68—69·5°/13 mm., n_D^{20} 1·4602; it provided an *α-naphthylurethane*, m. p. 82—84° (from ethanol–light petroleum) (Found: C, 63·15; H, 5·3; Cl, 11·6; N, 4·7. $C_{16}H_{16}O_3NCl$ requires C, 62·8; H, 5·2; Cl, 11·6; N, 4·6%). On catalytic hydrogenation [as for the isomer; cf. (a)], there was obtained 2-methoxybutan-1-ol, b. p. 141—144°, n_D^{20} 1·4154 [3 : 5-dinitrobenzoate, m. p. 60—62°, undepressed on admixture with an authentic specimen, m. p. 62—64° (Found: C, 48·8; H, 4·7; N, 9·55. Calc. for $C_{12}H_{14}O_7N_2$: C, 48·3; H, 4·7; N, 9·4%)].

(c) *Hydration.* The chloroepoxybutene (3·0 g.) was added to 98% formic acid (2 c.c.); the exothermic reaction was completed by further heating and then the formate was hydrolysed by boiling water. Distillation gave fractions: (1) (1·1 g.) b. p. 111—112°/15 mm., n_D^{20} 1·4790, and (2) (0·7 g.) b. p. 112—160°/15 mm., and a residue (1·0 g.). Fraction (1) provided the *phenylurethane*, m. p. 126—128° (from benzene) (Found: C, 60·3; H, 4·9; Cl, 9·55; N, 7·7. $C_{18}H_{17}O_4N_2Cl$ requires C, 59·9; H, 4·7; Cl, 9·85; N, 7·8%), of 3-chlorobut-3-ene-1 : 2-diol.

(d) *Reaction with hydrogen chloride.* (i) Chloroepoxybutene (5 g.) was added to an excess of ethereal hydrogen chloride; the reaction was exothermic. After 1 hr. the solution was diluted further with ether, washed with sodium hydrogen carbonate solution, dried, and distilled. The product (4·1 g.), b. p. 73—76°/14 mm., n_D^{20} 1·4932 (claimed by Petrov [5] to be 2 : 3-dichlorobut-3-en-1-ol), reacted very slowly with α-naphthyl *iso*cyanate, to give an

[7] Adams, Hawkins, Oldham, and Thompson, unpublished work.

α-naphthylurethane, m. p. 91—93° (Found: C, 58·4; H, 4·1; Cl, 22·3; N, 4·7. $C_{15}H_{13}O_2NCl_2$ requires C, 58·1; H, 4·2; Cl, 22·9; N, 4·5%).

(ii) The chloroepoxybutene (5 g.), stirred with concentrated hydrochloric acid (6 c.c.) for 1 hr. at 0°, gave the same dichlorobutenol (4·9 g.) as in (i), b. p. 73—77°/14 mm., n_D^{20} 1·4940 (α-naphthylurethane, m. p. and mixed m. p. 91—93°).

Reaction of 1 : 2-*Dichloro*-3 : 4-*epoxybutane with Hydrogen Chloride.*—(i) 1 : 2-Dichloro-3 : 4-epoxybutane (low-boiling isomer; 22 g.) was treated, with shaking and cooling, with an excess of ethereal hydrogen chloride. Distillation provided *erythro*-1 : 3 : 4-trichlorobutan-2-ol (25·8 g.), b. p. 108—109°/14 mm., n_D^{20} 1·5051; this alcohol had a hindered hydroxyl group (infrared spectrum) and gave a phenylurethane, m. p. 134—136° (Found: C, 44·7; H, 4·1; Cl, 35·5; N, 4·75. Calc. for $C_{11}H_{12}O_2NCl_3$: C, 44·5; H, 4·05; Cl, 35·9; N, 4·7%), identical with that isolated from one of the crude products of oxidation of 3 : 4-dichlorobut-1-ene by performic acid.

The *erythro*-trichlorobutanol (17·6 g.), suspended in water (10 c.c.), was treated with sodium hydroxide (4·0 g.) in water (8 c.c.), with stirring for 1 hr. at room temperature and at 40° for ½ hr. The solution was saturated with sodium chloride and extracted with ether; distillation provided a liquid (9·2 g.), b. p. 72·5—81°/13 mm., n_D^{20} 1·4742, and residue (4·5 g.). The distillate was a mixture of low-boiling 1 : 2-dichloro-3 : 4-epoxybutane (*ca.* 45%) and 1 : 4-dichloro-2 : 3-epoxybutane (*ca.* 55%) (infrared spectrum).

(ii) 1 : 2-Dichloro-3 : 4-epoxybutane (high-boiling isomer; 23·8 g.) was treated with ethereal hydrogen chloride as in (i), and gave threo-1 : 3 : 4-*trichlorobutan*-2-*ol* (27·0 g.), b. p. 106—107°/14 mm., n_D^{20} 1·5039 (Found: C, 26·8; H, 4·05; Cl, 59·7. $C_4H_7OCl_3$ requires C, 27·0; H, 3·94; Cl, 60·0%), having an associated hydroxyl group (infrared spectrum): it yielded a *phenylurethane*, m. p. 90—92·5° (from light petroleum) (Found: C, 44·7; H, 4·2; Cl, 36·3; N, 4·85%).

Treatment of the *threo*-trichlorobutanol with alkali gave a product, b. p. 71—73°/13 mm., n_D^{20} 1·4761, shown spectroscopically to be entirely high-boiling 1 : 2-dichloro-3 : 4-epoxybutane.

Reaction of 1 : 4-*Dichloro*-2 : 3-*epoxybutane with Hydrogen Chloride.*—This was carried out for comparison with the above. 1 : 4-Dichloro-2 : 3-epoxybutane [1,7] (20 g.) in ether (60 c.c.) was heated under reflux, and hydrogen chloride passed through the solution for 8 hr. The ethereal solution was further diluted with ether, washed with sodium hydrogen carbonate solution, dried, and distilled, to give 1 : 3 : 4-trichlorobutan-2-ol (20·5 g.), b. p. 104—105°/14 mm., n_D^{20} 1·5039; this was a mixture of isomers (spectrum) but it gave the phenylurethane, m. p. and mixed m. p. 136·5—139° (Found: C, 44·3; H, 4·0; Cl, 35·8; N, 4·8%), of the *erythro*-isomer.

This trichlorobutanol, when treated with alkali, gave a product, b. p. 69·5—74·5°/14 mm., n_D^{20} 1·4743, which contained (from the infrared spectrum) low-boiling 1 : 2-dichloro-3 : 4-epoxybutane (44%), the high-boiling isomer (34%), and 1 : 4-dichloro-2 : 3-epoxybutane (*ca.* 20%).

Preparation of 4-*Chloro*-2 : 3-*epoxybutan*-1-*ol.*—Sodium hydroxide (5 g.) in water (6 c.c.) and methanol (15 c.c.) was added, during 5 min., to a stirred solution of *erythro*-1 : 2-dichlorobutane-3 : 4-diol, and the mixture finally heated on the water-bath for 5 min. The cooled and filtered product was distilled, to give 4-*chloro*-2 : 3-*epoxybutan*-1-*ol* (13·3 g.), b. p. 106—110°/15 mm., n_D^{20} 1·4735 (Found: OH, 14·1%; epoxide equiv., 135·9. $C_4H_7O_2Cl$ requires OH, 13·9%; epoxide equiv., 122·5); the infrared spectrum confirmed the absence of unsaturation, carbonyl group, or tetrahydrofuran ring. It yielded a *phenylurethane*, m. p. 79—81° (Found: C, 55·0; H, 4·85; Cl, 14·5; N, 5·7. $C_{11}H_{12}O_3NCl$ requires C, 54·7; H, 5·0; Cl, 14·7; N, 5·8%).

The above preparation was also carried out in the absence of methanol.

Reactions of 4-*Chloro*-2 : 3-*epoxybutan*-1-*ol.*—(a) *Thermal decomposition.* The epoxide (5 g.) was heated at 220° for 1½ hr.; it became dark purple. Distillation gave *cis*-4-chlorotetrahydrofuran-3-ol (2 g.), b. p. 88—90°/15 mm., n_D^{20} 1·4871, and residue (1·8 g.). The product was identified spectroscopically.

(b) *Hydration.* The epoxide (5 g.) and formic acid (4 drops) were heated for ½ hr., and, after the addition of water (25 c.c.), boiled for a further 1½ hr. Distillation gave fractions (1) (1·2 g.) b. p. <140°/12 mm., and (2) (2·0 g.) b. p. 140—145°/12 mm., and a residue (1·0 g.).

Fraction (2) gave the *phenylurethane*, m. p. 186—188° (from ethanol), of *cis*-tetrahydrofuran-3 : 4-diol (Found: C, 63·55; H, 5·3; N, 8·3. $C_{18}H_{18}O_5N_2$ requires C, 63·2; H, 5·2; N, 8·2%), undepressed on admixture with the derivative of the tetrahydrofurandiol obtained by dehydration of *meso*-erythritol with sulphuric acid (cf. Reppe *et al.*[3]).

(c) *Alcoholysis.* (i) A mixture of the epoxide (5 g.), ethanol (25 c.c.), and toluene-*p*-sulphonic acid (trace) was heated under reflux for 57 hr. Distillation, after normal working up, gave

fractions (1) (1·3 g.) b. p. 85—88°/12 mm., n_D^{20} 1·4553, (2) (0·7 g.) b. p. 88—102°/12 mm., n_D^{20} 1·4579, and (3) (0·6 g.) b. p. 102—112°/12 mm., n_D^{20} 1·4620, and a residue (0·3 g.). The infrared spectra of these fractions showed them to contain a hindered hydroxyl group, a tetrahydrofuran ring, and an aliphatic ether, in agreement with *cis*-4-ethoxytetrahydrofuran-3-ol. Fraction (1) gave a *phenylurethane*, m. p. 73—75° (Found: C, 62·1; H, 7·0; N, 5·8. $C_{13}H_{17}O_4N$ requires C, 62·15; H, 6·8; N, 5·6%).

(ii) The epoxide (10 g.) was heated under reflux for 20 hr. with methanol (50 c.c.) containing sulphuric acid (3 drops). Distillation of the product gave fractions (1) (4·5 g.), b. p. 77—78°/13 mm., n_D^{20} 1·4544, and (2) (2·1 g.), b. p. 78—93°/13 mm., n_D^{20} 1·4620, and a residue (1·2 g.). The infrared spectrum of fraction (1) was in agreement with that of *cis*-4-methoxytetrahydrofuran-3-ol; fraction (2) contained mainly the same compound, but there was also present some of the *trans*-isomer (as from 3 : 4-epoxytetrahydrofuran). Fraction (1) gave a *phenylurethane*, m. p. 92—94° (from benzene–light petroleum, then ethanol) (Found: C, 61·1; H, 6·4; N, 5·9. $C_{12}H_{15}O_4N$ requires C, 60·8; H, 6·3; N, 5·9%).

(d) *Reaction with alkali.* (i) The epoxide (12·2 g.) was heated with sodium hydroxide (4 g.) in water (4 c.c.) and methanol (10 c.c.); the product was extracted with ether, and the extract gave a distillate (5·0 g.), b. p. *ca.* 220° (bath)/15 mm., and a residue (7·8 g.). The distillate, which contained an alkoxyl group (Zeisel), provided a *phenylurethane*, m. p. 204—205° (Found: C, 63·1; H, 5·5; N, 8·2. $C_{36}H_{27}O_7N_3$ requires C, 63·3; H, 5·5; N, 8·5%), depressed on admixture with the phenylurethane of *trans*-tetrahydrofuran-3 : 4-diol; the phenylurethane is probably a tris-derivative of a methoxybutanetriol.

(ii) The epoxide (12·2 g.) was added to a stirred solution of sodium methoxide (from 2·5 g. of sodium) in methanol (50 c.c.). The temperature was raised to 68° during ½ hr., and kept thereat for 2½ hr. The solution was cooled, treated with ethereal hydrogen chloride and then sodium hydrogen carbonate, filtered, and distilled, giving fractions (1) (1·0 g.) b. p. 94—109·5°/13 mm., n_D^{20} 1·4551, (2) (1·3 g.) b. p. 109·5—112·5°/13 mm., n_D^{20} 1·4488, (3) (3·3 g.) b. p. 112·5—116°/13 mm., n_D^{20} 1·4474, and (4) (1·4 g.) b. p. 116—135°/13 mm., n_D^{20} 1·4492, and a residue (2·0 g.). Infrared spectroscopy showed that these fractions were rather similar and contained hydroxyl and methoxyl functions. Fraction 3 was probably largely 3 : 4-*dimethoxybutane*-1 : 2-*diol* (Found: OH, 20·9; OMe, 39·6; vicinal OH, 70. $C_6H_{14}O_4$ requires OH, 22·7; OMe, 41·3%); it provided a *bisphenylurethane*, m. p. 158—160° (from ethanol–light petroleum) (Found: C, 61·8; H, 6·3; N, 7·35. $C_{20}H_{24}O_6N_2$ requires C, 61·85; H, 6·2; N, 7·2%).

(iii) The epoxide (1·7 g.) was heated under reflux for 7½ hr. with sodium hydroxide (0·7 g.) in water (20 c.c.). After neutralisation, the product was evaporated to dryness, and the residue extracted with ethanol. Distillation of the extract gave an oil (0·5 g.), b. p. 200—320° (bath)/0·5 mm.; crystallisation from ethanol, then methanol, gave *meso*-erythritol, m. p. and mixed m. p. 120—122°.

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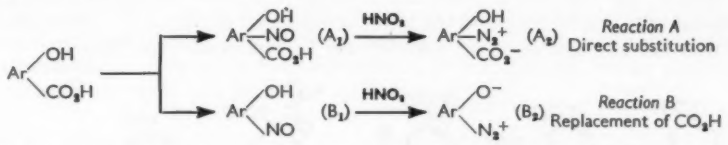
45 *The Direct Introduction of the Diazonium Group into Aromatic Nuclei. Part V.*[1] *The Action of Buffered Nitrous Acid on Aromatic Hydroxy-acids.*

By J. M. Tedder and G. Theaker.

Aromatic hydroxy-acids react with buffered nitrous acid in two ways, both leading to diazonium salts. The simpler is direct introduction of the diazonium group as observed with other phenolic compounds; but for *o*- or *p*-hydroxy-acids this reaction is wholly or partly superseded by decarboxylation and the diazonium group replaces the ejected carboxyl group. *p*-Hydroxycinnamic and caffeic acid are likewise decarboxylated, but attempts to prepare ethylenediazonium salts by this means have not been successful.

Part IV of this series [1] describes the reaction of phenols with buffered nitrous acid to yield diazonium salts. When this work was extended, it was found that some aromatic hydroxy-acids are decarboxylated by nitrous acid. Decarboxylation of some hydroxynaphthoic acids has been known for a long time,[2] the products being the nitrosonaphthols formed by the replacement of the ejected carboxyl by a nitroso-group. When the resulting nitroso-naphthol or -phenol is not specially stabilised in the quinone monoxime form (cf. Part IV) it would be expected to react with more nitrous acid to yield a diazonium salt. The first report of such a reaction comes recently from Nemodruk.[3] It will be clear, therefore, that when an aromatic hydroxy-acid reacts with nitrous acid any of four products may be formed:



The results of treating six hydroxy-acids with buffered nitrous acid as previously described [1] are in the annexed Table.

Reaction of hydroxy-acids (0·01 *mole*) *with buffered nitrous acid* ($NaNO_2$ 0·145 *mole* + HCl 0·04 *mole*) *in aqueous acetone.*

Acid	Conditions		Products (%) A_1	A_2	B_1	B_2
Salicylic	6 hr.	20°	—	17·5	—	48·5
m-Hydroxybenzoic	30½ hr.	20°	—	39·5	—	—
p-Hydroxybenzoic	18 hr.	20°	—	Trace	—	86·0
4-Hydroxy-3-nitrobenzoic	21 hr.	20°	—	—	—	42
2-Hydroxy-1-naphthoic	43 hr.	0°	—	—	85	Trace
3-Hydroxy-2-naphthoic	24 hr.	20°	?	18	—	—
	2 hr.	0°	53	Trace	—	—

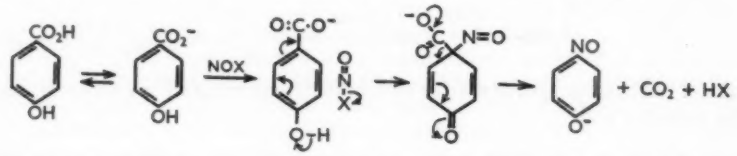
The reaction of salicylic acid with buffered nitrous acid has been the subject of five contradictory publications. A German patent claimed preparation of 5-nitrososalicylic acid by direct nitrosation; [4] Friedländer, recording this patent, expresses scepticism [4] and Lésniański [5] reported that the only product was *o*-nitrosophenol; [5] however, Gulinov [6]

[1] Part IV, Tedder and Theaker, *J.*, 1958, 2573.
[2] Nietzki and Guiterman, *Ber.*, 1887, **20**, 1274; Reverdin and de la Harpe, *Ber.*, 1883, **26**, 1279; Oddo and Mameli, *Atti Accad. Lincei*, 1901, **10**, II, 240.
[3] Nemodruk, *Zhur. obshchei Khim.*, 1956, **26**, 3283.
[4] G.P. 48,491; *Friedländer*, 1891, **2**, 221.
[5] Lésniański, *Przemysl Chem.*, 1922, **6**, 349; *Chem. Zentr.*, 1923, IV, 496.
[6] Gulinov, *Zhur. Khim. prom.*, 1927, **4**, 909; *Chem. Abs.*, 1928, **22**, 3648.

claimed to have prepared 5-nitrososalicylic acid by a method similar to that patented. Nemodruk reported the principal product from salicylic acid to be *o*-diazophenol,[3] and Henry [7] again reported decarboxylation but failed to detect any diazonium salt. We find that none of these reports is completely correct and the reaction is more complicated than was suspected. In the absence of metal salts the reaction of salicylic acid with nitrous acid depends on the acidity of the medium, but in no circumstances is nitrososalicylic acid a major product. As indicated in the Table, in buffered nitrous acid the main products are the two diazonium salts, *o*-diazophenol and 5-diazosalicylic acid. Increasing the acidity of the medium slows the whole reaction and greatly decreases the proportion of *o*-diazophenol. In the presence of certain metal ions, *e.g.*, cupric, the reaction is complicated: some nitrososalicylic acid can be isolated but the yield falls well short of that claimed by Gulinov and the nitrososalicylic acid is accompanied by diazosalicylic acid. No attempt has yet been made to define further the course of the reaction in the presence of metal ions.

It is reasonable that salicylic acid stands between *m*-hydroxybenzoic acid, which undergoes no decarboxylation, and *p*-hydroxybenzoic acid, which yields only decarboxylated product, as does 4-hydroxy-3-nitrobenzoic acid. It is of interest that the nitro-group decreases the rate of decarboxylation only slightly. The reactions of nitrous acid with 2-hydroxy-1- and 3-hydroxy-2-naphthoic acid to yield 1-nitroso-2-naphthol and 3-hydroxy-4-nitroso-2-naphthoic acid respectively have been reported,[2] but the presence of diazonium salts was not previously suspected.

To obtain some insight into the mechanism of the decarboxylation, the effects of acidity and of esterification and *O*-alkylation were investigated. Decarboxylation can be completely suppressed by raising the acidity of the medium, even with *p*-hydroxybenzoic acid. Neither methyl salicylate nor *p*-anisic acid is decarboxylated; the former gives a low yield of diazonium salt (reaction A), and the latter is recovered unchanged. These observations suggest that the mechanism of the reaction can be represented as follows:



The results described above made it seem possible that the reaction of 4-hydroxycinnamic acid with nitrous acid might yield the first of the, as yet unknown, ethylenediazonium salts:

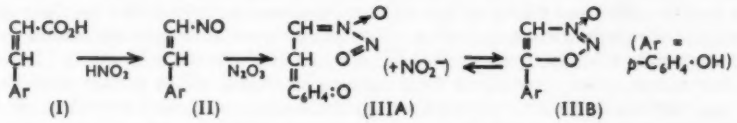
$$p\text{-HO}\cdot C_6H_4\cdot CH{:}CH\cdot CO_2H \longrightarrow p\text{-HO}\cdot C_6H_4\cdot CH{:}CH\cdot NO \longrightarrow p\text{-HO}\cdot C_6H_4\cdot CH{:}CH\cdot \overset{+}{N}{\equiv}N$$

Decarboxylation does occur, but no evidence to suggest appreciable yields of ethylenediazonium salt has been obtained. Prolonged treatment with buffered nitrous acid causes complete removal of the side-chain, and *p*-diazophenol is then the main product. With shorter reaction times and more acidic media traces of a diazonium salt, which may have been the ethylene compound, were detected, but far too little was obtained to make characterisation possible. Besides these diazonium salts an unidentified nitrogenous compound ($C_8H_6O_3N_2$) was isolated, to which we tentatively ascribe structures IIIA and B, partly on mechanistic grounds.

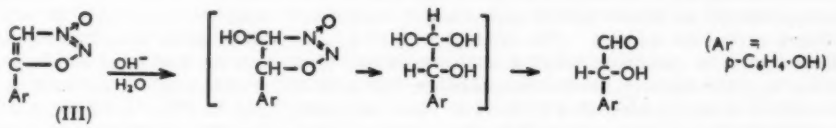
While this work was in progress Ziodrou *et al.*[8] reported that *p*-hydroxycinnamic acid with nitrous acid yielded *p*-hydroxymandelaldehyde. Although the isomeric **4** : ω-dihydroxyacetophenone had been previously reported, they did not compare their product with this compound, and the evidence that their compound was the aldehyde seemed to

[7] Henry, *J. Org. Chem.*, 1958, **23**, 648.
[8] Ziodrou, Meyer, and Fruton, *J. Amer. Chem. Soc.*, 1957, **79**, 4114.

need confirmation, particularly as repeating the experiment gave different results. This re-investigation, including the synthesis of 4 : ω-dihydroxyacetophenone, leads us to believe that *p*-hydroxymandelaldehyde is in fact one of the products from the treatment



of *p*-hydroxycinnamic acid with nitrous acid. The dihydroxyacetophenone and the compound obtained by Ziodrou *et al.* are not identical, but they give the same osazone.



The aldehyde is probably formed *via* our compound (III) in the manner indicated. Treat- of compound (III) with sodium hydrogen carbonate solution (it is stable in acid solution) rapidly yields a carbonyl compound giving a 2 : 4-dinitrophenylhydrazone identical with that from the compound of Ziodrou *et al.*, together with a compound containing no nitrogen possibly formed by the dimerisation of the aldehyde in alkaline solution. Treatment of compound (III) with 0·2N-sodium nitrite (conditions to simulate the experiment of Ziodrou *et al.*) slowly yields the aldehyde without the dimer.

We also briefly investigated the action of nitrous acid on caffeic acid in the hope that if an unstable diazonium salt was formed it would couple intramolecularly to yield 6 : 7-dihydroxycinnoline. Caffeic acid is decarboxylated by nitrous acid, but no product having the properties of the expected cinnoline was detected.

Experimental

Salicylic Acid.—Salicylic acid (1·38 g.), dissolved in acetone (20 c.c.) and water (150 c.c.), was treated with sodium nitrite (10 g.) and 2N-hydrochloric acid (15 c.c.). After 6 hr. at 20° a sample (50 c.c.) was withdrawn, treated with sulphamic acid to remove the excess of nitrite, and extracted with ether. The yellow ether extract contained a trace of a diazo-compound, but yielded mainly unchanged salicyclic acid (0·09 g., 24%), m. p. 153—155°. The aqueous layer was neutralised with sodium carbonate, treated with excess of resorcinol, adjusted to pH 10, and left for 2 hr. The mixture of dyes was precipitated by acidification and isolated by filtration (0·43 g.; m. p. 196—200°). A portion of the mixture (0·2 g.) was suspended in sodium hydrogen carbonate solution and extracted with ether until the extracts were almost colourless. The combined extracts on evaporation yielded crude *o-hydroxyphenylazoresorcinol* (0·14 g.; m. p. 198—201°), which recrystallised from aqueous methanol as a yellow-orange powder, m. p. 203—204°, $\lambda_{max.}$ 425 mμ (in EtOH) (Found: C, 62·7; H, 4·7; N, 12·3. $C_{12}H_{10}O_3N_2$ requires C, 62·6; H, 4·4; N, 12·2%). Authentic *o*-hydroxyphenylazoresorcinol, prepared from *o*-aminophenol by diazotisation and coupling, had $\lambda_{max.}$ 425 mμ (in EtOH) and m. p. and mixed m. p. 203—204°. In both cases the pure dye gave a yellow-brown colour in concentrated sulphuric acid which became orange on dilution. The dye retained in the sodium hydrogen carbonate solution after the ether-extractions was isolated by acidification and a fresh ether-extraction. The crude *3-carboxy-4-hydroxyphenylazoresorcinol* obtained by evaporation of the ether (0·06 g.; no m. p.; decomp. >210°) was purified by recrystallisation from aqueous methanol (Found: C, 56·9; H, 3·9; N, 10·4. $C_{13}H_{10}O_5N_2$ requires C, 56·9; H, 3·7; N, 10·2%). The orange-red powder had $\lambda_{max.}$ 387 mμ (in EtOH) but no definite m. p. The authentic dye prepared from 5-aminosalicylic acid had identical properties. The pure dyes gave bright orange colours in concentrated sulphuric acid. When the experiment was repeated

using more concentrated conditions (water 100 c.c.; acetone 25 c.c.) the salicylic acid diazo-oxide [0·2 g.; m. p. 175—180° (decomp.)] separated after 26 hr.

m-*Hydroxybenzoic Acid.*—*m*-Hydroxybenzoic acid (1·38 g.) was treated as in the previous experiment. After 7·5 hr. a sample (50 c.c.) yielded unchanged *m*-hydroxybenzoic acid (0·27 g., 73%; m. p. 197—198°) and 0·12 g. of dye with no definite m. p. After 30·5 hr. the yield of dye from a similar sample had risen to 0·31 g. The crude dye was completely soluble in sodium hydrogen carbonate solution, from which no dye could be extracted with ether. *2-Carboxy-4-hydroxyphenylazoresorcinol* crystallised from aqueous methanol as the monohydrate in orange needles, $\lambda_{max.}$ 430 mμ (in EtOH); it had no m. p. but decomposed above 275° (Found: C, 53·7; H, 4·3; N, 9·8; H_2O, 5·4. $C_{13}H_{10}O_5N_2,H_2O$ requires C, 53·4; H, 4·1; N, 9·6; H_2O, 6·2%), and gave a bright orange colour in concentrated sulphuric acid.

p-*Hydroxybenzoic Acid.*—*p*-Hydroxybenzoic acid (1·38 g.) in acetone (10 c.c.) and water (65 c.c.) was treated with sodium nitrite (10 g.) and 2N-hydrochloric acid (20 c.c.). A sample (25 c.c.) treated as before yielded a dye which was almost completely insoluble in sodium hydrogen carbonate solution. The crude dye (0·52 g.), m. p. 220—225°, was extracted with sodium hydrogen carbonate solution and crystallised from aqueous methanol as dark red needles, $\lambda_{max.}$ 385 mμ, m. p. alone or in admixture with authentic *p*-hydroxyphenylazoresorcinol [1] 226—227° (Found: C, 62·5; H, 4·7; N, 11·9. Calc. for $C_{12}H_{10}O_3N_2$: C, 62·6; H, 4·4; N, 12·2%). The infrared absorption spectrum (KBr disc) of the product was identical with that of *p*-hydroxyphenylazoresorcinol.

4-*Hydroxy-3-nitrobenzoic Acid.*—4-Hydroxy-3-nitrobenzoic acid (0·12 g.) was treated in acetone (2 c.c.) and water (7 c.c.) with sodium nitrite (0·7 g.) and 2N-hydrochloric acid (1·7 c.c.) and filtered after 21 hr. at 20°. The precipitate (0·04 g.) consisted of unchanged starting material, m. p. and mixed m. p. 178—180°. The filtrate was treated with ice and excess of sulphamic acid solution, then neutralised with aqueous sodium carbonate. Excess of resorcinol was added and the solution rendered alkaline (pH ~10) with sodium hydroxide solution. Coupling was allowed to proceed for 2 hr. and the dye was isolated after acidification. The crude dye (0·05 g.), m. p. 105—210°, recrystallised from aqueous acetone as orange-red needles, m. p. alone or in admixture with 4-hydroxy-3-nitrophenylazoresorcinol [1] 216—218°, $\lambda_{max.}$ 386 mμ (in EtOH).

2-*Hydroxy-1-naphthoic Acid.*—2-Hydroxy-1-naphthoic acid (0·5 g.) was treated in acetone (30 c.c.) and water (50 c.c.) with sodium nitrite (2·7 g.) and 2N-hydrochloric acid (5·3 c.c.). The reactants were maintained at 0° and a yellow precipitate soon developed. After 43 hr. the mixture was filtered. The precipitate (0·37 g.), m. p. 80—90° (decomp.), was insoluble in aqueous sodium hydrogen carbonate. It recrystallised from aqueous methanol, and the purified material had m. p. 107—108° alone or mixed with 1-nitroso-2-naphthol. The filtrate contained only a trace of diazonium salt together with some further nitrosonaphthol.

The above experiment was repeated at 20°. After 28 hr. a small precipitate was filtered off (0·04 g.; m. p. 171—173°). This product, which had the properties of a nitroso-compound, was not investigated. The filtrate was treated with excess of sulphamic acid, neutralised with sodium carbonate, and coupled with resorcinol as before. The yield of dye was too small to be isolated by filtration and the acidified solution was extracted with chloroform. Purification was achieved on an alumina column; unchanged resorcinol and nitrosonaphthol were eluted with ether, and the dye was recovered by washing the alumina with dilute hydrochloric acid and then extracting the washing with ether. The dark solid had m. p. 200° (decomp.), $\lambda_{max.}$ 525 mμ (0·004 g./l. in ethanol), or $\lambda_{max.}$ 485—490 and 520 mμ (0·01 g./l. in ethanol); it gave a red-purple colour in concentrated sulphuric acid. These properties are identical with those of the dye obtained by coupling the diazonium salt, formed when β-naphthol is treated with nitrous acid, with resorcinol.[1]

3-*Hydroxy-2-naphthoic Acid.*—3-Hydroxy-2-naphthoic acid (1·88 g.) was treated in acetone (30 c.c.) and water (100 c.c.) with sodium nitrite (10 g.) and 2N-hydrochloric acid (20 c.c.) at 0°. A brown precipitate (1·15 g.) which began to be formed almost at once was filtered off after 2 hr. It was soluble in sodium hydrogen carbonate solution with evolution of carbon dioxide, and gave the characteristic reactions of a nitroso-compound; it had m. p. 179—183° (3-hydroxy-4-nitroso-2-naphthoic acid [9] has m. p. 185°).

The experiment was repeated at 20°, 3-hydroxy-2-naphthoic acid (0·94 g.) was treated in acetone (15 c.c.) and water (50 c.c.) with sodium nitrite (5 g.) and 2N-hydrochloric acid

[9] Kostanecki, *Ber.*, 1893, **26**, 2897.

(10 c.c.). A small dark precipitate was formed and after 24 hr. the mixture was poured on ice (100 g.) and treated with sulphamic acid. The mixture was neutralised with sodium carbonate, and excess of resorcinol was added. The solution was adjusted to pH ~10 with sodium hydroxide solution and left for 5 hr. The crude dye (0·30 g.) was isolated by acidification and filtration, and recrystallised from aqueous methanol to yield *3-carboxy-2-hydroxy-1-naphthylazoresorcinol monohydrate* as a dark purple powder, m. p. indef., decomp. >210°, $\lambda_{max.}$ 505 mμ (in EtOH) (Found: C, 59·3; H, 4·1; N, 8·0; H_2O, 4·5. $C_{17}H_{13}O_5N_2.H_2O$ requires C, 59·6; H, 4·1; N, 8·2; H_2O, 5·3%).

Salicylic Acid in Acid Conditions.—Salicylic acid (0·5 g.) was treated in acetone (15 c.c.) and water (100 c.c.) with sodium nitrite (1·0 g.) and 2N-hydrochloric acid (10 c.c.) at 20°. After 27 hr. a 50 c.c. sample was treated as in the experiment under buffered conditions. The sample yielded crude resorcinol dye (0·07 g.), no m. p., decomp. >210°, and unchanged salicylic acid (0·15 g., 75%), m. p. 152—155°. The dye was completely soluble in sodium hydrogen carbonate solution and its properties were identical with those of 3-carboxy-4-hydroxyphenylazoresorcinol described above.

p-*Hydroxybenzoic Acid in Acid Conditions.*—*p*-Hydroxybenzoic acid (1 38 g.) was treated in acetone (15 c.c.) and water (150 c.c.) with sodium nitrite (2·8 g.) and 2N-hydrochloric acid (30 c.c.) at 20°. After 48 hr. a sample (50 c.c.) was withdrawn and treated as before. The resorcinol dye (0·02 g.) obtained from the sample was completely soluble in sodium hydrogen carbonate solution; it had no definite m. p., $\lambda_{max.}$ 397 mμ (in EtOH), and gave an orange colour in concentrated sulphuric acid. It was not characterised further.

Methyl Salicylate.—Methyl salicylate (1·52 g.) was treated in acetone (70 c.c.) and water (50 c.c.) with sodium nitrite (10 g.) and 2N-hydrochloric acid (20 c.c.). After 8·5 hr. at 20° a sample (40 c.c.) was withdrawn, treated with excess of sulphamic acid, and extracted with ether. The ether layer contained the unchanged methyl salicylate (80%) and the aqueous layer was neutralised with aqueous sodium carbonate and coupled with resorcinol as before. The crude dye (0·08 g.), m. p. 210—214°, was isolated after acidification and recrystallised from aqueous methanol, to yield *4-hydroxy-3-methoxycarbonylphenylazoresorcinol* as orange needles, m. p. 217°, giving a light yellow-orange colour in concentrated sulphuric acid (Found: C, 58·5; H, 4·3; N, 10·1. $C_{14}H_{12}O_5N_2$ requires C, 58·3; H, 4·2; N, 9·7%).

p-*Anisic Acid.*—*p*-Anisic acid (1·52 g.) was treated in acetone (50 c.c.) and water (25 c.c.) with sodium nitrite (10 g.) and 2N-hydrochloric acid (20 c.c.). After 24 hr. unchanged anisic acid (m. p. 182—184°) separated. Even after 7 days only a trace of diazonium salt could be detected.

4-Hydroxycinnamic Acid.—(a) *In standard buffered solutions.* 4-Hydroxycinnamic acid (2·5 g.) was treated in acetone (50 c.c.) and water (75 c.c.) with sodium nitrite (15 g.) and 2N-hydrochloric acid (30 c.c.). After 48 hr. at 0°, the mixture was poured on ice (100 g.) and treated with sulphamic acid. The solution was filtered; the brown precipitate (0·1 g.), which contained nitrogen, had the properties of a diazo-oxide but was not characterised further. The filtrate was neutralised with aqueous sodium carbonate and treated with excess of resorcinol before being brought to pH ~10 with sodium hydroxide, set aside for 2 hr., and acidified. The crude dye (1·84 g.), m. p. 160—180°, was shown by paper chromatography to contain at least two products. It (0·6 g.) was dissolved in ether (100 c.c.) and extracted twice with saturated sodium hydrogen carbonate (25 c.c.). Evaporation left a red powder (0·48 g.), m. p. 219—221°, raised by recrystallisation from aqueous methanol to 225—226°. This did not depress the m. p. of *p*-hydroxyphenylazoresorcinol and the ultraviolet ($\lambda_{max.}$ 386 mμ in EtOH) and infrared spectra (KBr disc) and colours in concentrated sulphuric acid were identical (Found: C, 62·5; H, 4·6; N, 12·0. Calc. for $C_{12}H_{10}O_3N_2$: C, 62·6; H, 4·4; N, 12·2%). If the crude dye after the extraction with sodium hydrogen carbonate consisted mainly of *p*-hydroxyphenylazoresorcinol, this corresponds to a 42·0% yield. The sodium hydrogen carbonate washings from the above were acidified and extracted with ether; evaporation of the ether left a slightly tarry red solid (0·10 g.), m. p. >150° (decomp.), whose ultraviolet spectrum showed it to be largely *p*-hydroxyphenylazoresorcinol, together with another uncharacterised dye ($\lambda_{max.}$ 431 mμ in EtOH).

(b) *Experiment of Ziodrou* et al.[8] 4-Hydroxycinnamic acid (1·0 g.) was treated in dioxan (17 c.c.) with sodium nitrite (0·82 g.) in water (17 c.c.), followed by 2N-hydrochloric acid (3·3 c.c.). After 1·5 hr. at 20° the mixture was evaporated to dryness in a vacuum. The yellow-brown solid was extracted with hot acetone (3 × 25 c.c.), and the combined extracts

were evaporated to leave a red oil (0·25 g.) (at this stage Ziodrou *et al.* describe a solid which after washing with cold water and acetone melted at 181—183°). A solution of the oil in alcohol gave a 2 : 4-dinitrophenylhydrazone, m. p. 277—279° (Found: C, 51·2; H, 3·9; N, 17·5. Calc. for $C_{14}H_{12}O_6N_4$: C, 50·6; H, 3·6; N, 16·9%); Ziodrou *et al.* report *p*-hydroxymandelaldehyde 2 : 4-dinitrophenylhydrazone, m. p. 280° (decomp.).

(c) 4-Hydroxycinnamic acid (1·0 g.) was treated in acetone (10 c.c.) and water (20 c.c.) with sodium nitrite (0·82 g.) and 2N-hydrochloric acid (3·3 c.c.). After 2 hr. at 0° the mixture was poured on ice (100 g.), treated with sulphamic acid solution, neutralised with sodium hydrogen carbonate, and exhaustively extracted with ether. The aqueous layer was treated with resorcinol and coupled in the usual way; only a trace of dye was formed. Evaporation of the ether left a brown tar (0·6 g.) which largely solidified on the addition of methanol. Four recrystallisations from methanol yielded 5-p-*hydroxyphenyl*-1 : 2 : 3-*oxadiazole* 3-*oxide* (III) as cream-coloured needles, m. p. 196—197° (Found: C, 54·2; H, 3·4; N, 15·5. $C_8H_6O_3N_2$ requires C, 54·0; H, 3·4; N, 15·7%), $\lambda_{max.}$ 248 mμ (strong) and 292 mμ (weak) (in EtOH). The infrared spectrum (KBr disc) was complicated but had no carbonyl band and a strong band at 1399 cm.$^{-1}$ was consistent with the (N:N·O) grouping proposed. A portion of the substance was refluxed with acetic acid for 2 hr. and then diluted with water and allowed to crystallise. This process was repeated three times. The resultant white needles had m. p. 182—187° (Found: C, 54·0; H, 3·4; N, 15·1%), *i.e.*, were apparently unchanged. A solution of compound (III) gave no reaction with 2 : 4-dinitrophenylhydrazine hydrochloride solution. The oxide (0·027 g.) was treated with saturated sodium hydrogen carbonate solution at 50° for 10 min. It slowly dissolved and the solution became orange-red. The solution was cooled and acidified, giving a yellow precipitate (m. p. 250—255°). This contained no nitrogen and on recrystallisation had m. p. 282° [Found (on 2·15 mg.): C, 59·1; H, 5·9%]. The filtrate was treated with 2 : 4-dinitrophenylhydrazine hydrochloride solution: a hydrazone (m. p. 262—270°) was formed. On recrystallisation from methanol it had m. p. 271—278° not depressed on admixture with *p*-hydroxymandelaldehyde 2 : 4-dinitrophenylhydrazone (Found: N, 17·3. Calc. for $C_{14}H_{12}O_6N_4$: N, 16·9%). The oxide (III), heated with 0·2N-sodium nitrite, yielded the aldehyde (as indicated by hydrazone formation) slowly, but gave none of the yellow precipitate described above.

4 : ω-*Dihydroxyacetophenone*.—ω-Chloro-*p*-hydroxyacetophenone was prepared from chloroacetyl chloride and anisole according to the method of Robertson and Robinson,[10] but with light petroleum (b. p. 40—60°) in place of carbon disulphide. Alkaline hydrolysis followed by acidification yielded a ketone, m. p. 302—306° (Found: C, 70·8; H, 5·3%) [2 : 4-dinitrophenylhydrazine, m. p. 270—272° (Found: N, 12·9%)], which clearly was not the desired compound but possibly a dimer of unknown structure. The sodium salt of 4 : ω-dihydroxyacetophenone was then prepared from the ω-chloro-*p*-hydroxyacetophenone *via* ω-acetoxy-*p*-hydroxyacetophenone according to the method of Robertson and Robinson.[10] Treated with aqueous hydrochloric acid this salt yielded the same high-melting ketone as before, but when the sodium salt suspended in ether was treated with a slight excess of concentrated hydrochloric acid, evaporation of the ether, after removal of the salt, yielded the desired *ketone*, m. p. 160—165°. Recrystallised twice from toluene, it had m. p. 170—172° (Found: C, 62·7; H, 5·5. $C_8H_8O_3$ requires C, 63·1; H, 5·3%), and gave a 2 : 4-*dinitrophenylhydrazone*, m. p. 246—249° (Found: N, 17·2. $C_{14}H_{12}O_6N_4$ requires N, 16·9%), and osazone, m. p. 202—203° (Found: C, 72·2; H, 5·6; N, 16·9. Calc. for $C_{20}H_{18}ON_4$: C, 72·7; H, 5·5; N, 16·9%). Ziodrou *et al.*[8] report the osazone from *p*-hydroxymandelaldehyde to have m. p. 198—199°. The ketone was soluble in water.

Department of Chemistry, University of Sheffield. [*Received, September 13th*, 1958.]

[10] Robertson and Robinson, *J.*, 1928, 1460.

46. *Unstable Intermediates. Part I. Photochemical Reactions in Rigid Glasses.*

By M. C. R. Symons and M. G. Townsend.

Highly reactive intermediates, formed by photolysis with ultraviolet light (2537 or 3650 Å), of dilute solid solutions of photosensitive compounds are often stabilised by being trapped in the glass. These intermediates, which are often free radicals, have been studied by spectrometric and electron-spin resonance methods: they are quite stable provided the glass is rigid, but are rapidly decomposed otherwise. The solvents included a variety of alcohols, carboxylic acids, saturated hydrocarbons, and vinyl compounds. The solutes included hydrogen peroxide, benzoyl peroxide, di-*tert.*-butyl peroxide, $\alpha\alpha'$-azo*iso*butyronitrile, and ethyl iodide. The nature of the trapped intermediates is discussed in terms of a generalised scheme for photolysis in rigid media.

When reaction mechanism is considered it is often necessary to postulate the formation of intermediates which, because of their high reactivity, are never present in isolable or even in detectable quantities, and whose presence is therefore inferred because the proposed mechanism agrees with expectation or because the results of kinetic studies are adequately accommodated thereby. By suitable modification of the environment it is sometimes possible to build up concentrations of such intermediates sufficiently to permit of direct detection and study, particularly spectrometrically. We have studied how this may be accomplished; in particular, ultraviolet spectrophotometry and magnetic techniques are used to detect and study the intermediates.[1]

Lewis and Lipkin [2] described the changes in the electronic absorption spectra of organic molecules in dilute solution in rigid glasses at 70° K after ultraviolet irradiation. They obtained good evidence both for photodissociation into radicals and for photoionisation. Since then, spectrophotometry [3-5] and electron-spin resonance techniques [6] have also been used to study such photolysed glasses.[6] These two techniques being complementary, we aimed to combine them to examine the nature of the photochemical reactions in rigid media.

Experimental

Materials.—Hydrogen peroxide (90%, free from stabilisers) was kindly supplied by Laporte Chemicals Ltd. Water was distilled from alkaline permanganate, and other solvents were "AnalaR" or purified by standard procedures.

Glasses.—For electron-spin resonance studies, clear glasses were not essential, and provided a small fraction of the incident light penetrated some distance into the specimen, seemingly opaque solids could be used. For spectrophotometry studies it was necessary to obtain clear glasses, rigid at 100° K (the lowest temperature suitable for measurement with our apparatus), which did not shatter badly over a considerable time interval. These conditions were achieved for alcohols by adding small quantities of syrupy phosphoric acid, and for glycols and acids by adding up to 50% of water. *cyclo*Hexane (10%) was added to *cyclo*hexanol to prevent cracking. In cases for which no such additive was required, it was confirmed that their presence did not affect the characteristic changes in ultraviolet spectra.

Solute concentrations were varied in the range 10^{-1}—10^{-3}M.

Electron-spin Resonance Measurements.—These were made as described previously.[6] Spectra were recorded as the first derivative of the absorption band, the sample, contained in a thin

[1] Cf. Symons, *J.*, 1957, 387, 2186, 2440; Ingram and Symons, *J.*, 1957, 2437.
[2] Lewis and Lipkin, *J. Amer. Chem. Soc.*, 1942, **64**, 2801.
[3] Norman and Porter, *Proc. Roy. Soc.*, 1955, *A*, **230**, 399.
[4] (*a*) Sowden and Davidson, *J. Amer. Chem. Soc.*, 1956, **78**, 1291; (*b*) Linschitz, Berry, and Schweitzer, *ibid.*, 1954, **76**, 5833.
[5] Symons and Townsend, *J. Chem. Phys.*, 1957, **25**, 1299.
[6] Gibson, Ingram, Symons, and Townsend, *Trans. Faraday Soc.*, 1957, **53**, 914.

walled quartz tube, being placed directly in an H_{014} 3 cm. wavelength rectangular cavity cooled by liquid nitrogen.[6]

Spectrophotometric Measurements.—These were made by using a Unicam S.P. 500 spectrophotometer modified for use at low temperature. The irradiated glasses were contained in a cell constructed to avoid breakage caused by cracking of the glass consisting of two fused silica plates recessed into the bottom of a Perspex rod and enclosing an oval hole cut in the rod. The cell was filled by partly removing one plate, completely filling the cell, replacing the plate, and then immersion in liquid nitrogen. This procedure made it unnecessary to ensure that the cell did not leak slightly, and any reaction between the Perspex walls and the solution was reduced to a minimum.

The cell housing, described in detail elsewhere,[7] consisted of a box of black Perspex containing baffles through which a stream of cold gas could be passed. The cell, immersed in liquid nitrogen, contained in a Dewar flask attached to the bottom of the cell housing could be raised into the light path for measurement, and a heater, also immersed in the liquid nitrogen, could be regulated so that the rate of flow of cold nitrogen gas past the cell, and hence the temperature of the cell, could be controlled accurately.

The optical densities of the glasses, before and after irradiation, were measured against air. In order to obtain the spectra required, the experiments were repeated, under the same conditions, for pure solvent. These spectra were then subtracted after a suitable correction had been made for differences in the degree of cracking of the glasses by subtracting a zero reading, obtained by measurement in a region of the spectrum in which no specific absorption occurred, from optical densities at all wavelengths. (This correction depends upon the arbitrary assumption that scattering due to cracking is not a function of wavelength: thereby, the errors introduced are largely cancelled, since the corrections required were usually very similar.)

The lowest temperatures attained, measured by a thermocouple in the cell holder, were about 20° above the b. p. of the coolant. Whilst this was satisfactory for studying the most interesting spectra, it was not cold enough for studying spectra of species formed in certain solid hydrocarbon glasses such as those used by other workers.[3,4a]

Photolyses.—Glasses in the cells immersed in liquid nitrogen, were irradiated with light, consisting largely of 2537 or 3650 Å wavelengths for periods of up to 6 hr. The sources were a low-pressure 150 w mercury arc with a discharge in the shape of a finger 4 in. long and jacketed by an evacuated quartz envelope (2537 Å), and a medium-pressure, 250 w mercury arc used in conjunction with an aluminised mirror. The low-pressure arc was immersed directly in the coolant, the evacuated envelope effectively preventing heat transfer which would otherwise extinguish the lamp.[6]

The small five-line electron-spin resonance signal detected after irradiation of ethanol glasses at 2537 Å is ascribed to ethanol radicals, $CH_3{\cdot}\dot{C}H{\cdot}OH$. These may arise from a variety of causes: (i) As the result of direct photolysis according to the equations:

$$CH_3{\cdot}CH_2{\cdot}OH \longrightarrow CH_3{\cdot}\dot{C}H{\cdot}OH + H{\cdot}$$

$$H{\cdot} + CH_3{\cdot}CH_2{\cdot}OH \longrightarrow H_2 + CH_3{\cdot}\dot{C}H{\cdot}OH$$

It is unlikely that 2537 Å light could accomplish this since there is no electronic absorption band in this region. However, low-pressure mercury lamps emit weakly in the 1900 Å region, where alcohols absorb strongly. Since ethanol exposed to ionising radiation gives a similar five-line spectrum [8,9] it is possible that this is the process involved.

(ii) The radicals may arise by abstraction of hydrogen by photo-excited oxygen molecules fortuitously present in solution, or by hydrogen-atom exchange between ethanol and traces of acetaldehyde:

$$CH_3{\cdot}CH_2{\cdot}OH + CH_3{\cdot}CHO \longrightarrow 2CH_3{\cdot}\dot{C}H{\cdot}OH$$

Work now being undertaken may yield definite conclusions.

Similar electron-spin resonance spectra were sometimes recorded after exposure of alcoholic solutions to 2537 Å light. These signals were compared with those obtained from the solvent

[7] Symons and Townsend, *Spectrovision*, 1957, **4**, 5.
[8] Gordy and Luck, *J. Amer. Chem. Soc.*, 1956, **78**, 3240.
[9] Alger, Anderson, and Webb, *J. Chem. Phys.*, in the press.

alone under identical conditions, and if this proved to be appreciably less intense it was assumed that electron-spin resonance results gave no evidence for the formation of radicals from the substrate. This assumption, whilst open to question, will be made throughout the discussion. No electron-spin resonance signal was detected after irradiation of solvent with 3650 Å light, so this difficulty does not then arise.

Results

Spectral details are summarised in the Table. Representative spectra are reproduced in Figs. 1, 2, and 3.

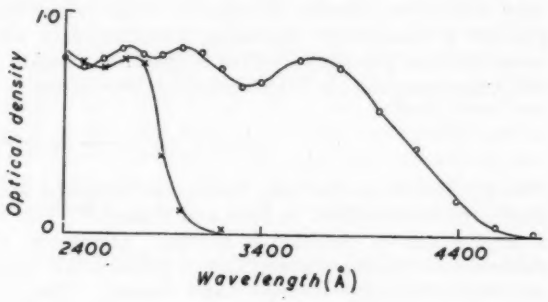


FIG. 1. *Spectrum of a solid solution of benzoyl peroxide in ethanol.*
–○– After irradiation with 2537 Å light.
–×– After warming to room temperature.

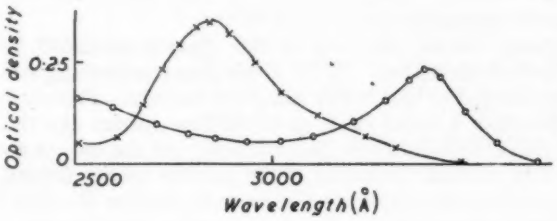


FIG. 2. *Spectrum of a solid solution of αα′-azoisobutyronitrile in ethanol.*
–○– Before irradiation.
–×– After irradiation with 3650 Å light.

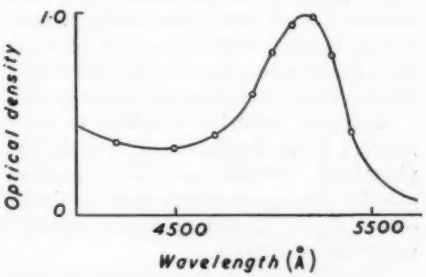


FIG. 3. *Spectrum of a solid solution of hydrogen peroxide in ethanol after irradiation with* 3650 Å *light.*

Photolysis of Hydrogen Peroxide.—In primary and secondary alcohols a violet colour appears after prolonged irradiation of dilute solutions. An extinction coefficient of about 300 was estimated for the band at 520 mμ by determination of the peroxide concentration before and after irradiation. This value is a lower limit because a radical-induced decomposition of residual hydrogen peroxide probably occurred during warming-up.

There is considerable speculation regarding the nature of the violet species. The following experiments were carried out in an attempt to clarify the situation (see p. 268). (*a*) The violet glasses were exposed to visible light for prolonged periods: no bleaching or change in the electron-spin resonance spectrum was detected. (*b*) Ethanol solutions were saturated with anhydrous lithium chloride: no change from the normal spectrum was

detected after irradiation. (*c*) A solution of hydrogen peroxide in ethanol was degassed by repeated freezing under vacuum (10^{-4} mm.), and the container was sealed under vacuum before irradiation. Again, no change in the properties of the irradiated sample was apparent.

Striking evidence for the conversion of one unstable species into another before completion of reaction was obtained by studying the effect of a gradual increase in temperature upon the visible spectra of violet glasses containing excess of hydrogen peroxide. By slowly decreasing the rate of flow of cold gas through the cell-housing, it was possible to obtained a temperature gradient along the cell such that the lower portion remained violet, the centre became bright yellow, and the uppermost portion colourless. It proved very difficult to measure the spectra of the yellow glasses because it was impossible to prevent a cloudiness's appearing simultaneously with the yellow colour. However, in one attempt a marked shoulder in the 3700 Å region was recorded. It is suggested that the yellow compound is HO_2· formed by the reaction

$$R_2\dot{C}{\cdot}OH + H_2O_2 \longrightarrow R_2CH{\cdot}OH + HO_2{\cdot}$$

This reaction is energetically favourable compared with the alternative hydroxyl-radical displacement postulated by Merz and Waters.[10] The yellow colour is only observed when a large excess of peroxide is present. Livingston, Ghormley, and Zeldes[11] observed electron-spin resonance absorption in yellow solids obtained by condensing products from an electric discharge through water vapour. They consider that their results are best interpreted by the assumption that the paramagnetic species is HO_2·.

Another example of colour change during softening of the glass is furnished by irradiated disulphur dichloride in methyl*cyclo*hexane. At 77° K this glass was intensely red, but on careful warming, the colour changed to blue before being lost entirely. Photolysis of a similar solution in 3-methylpentane, a softer glass, gave the blue species directly. Electron resonance studies showed that the glasses were paramagnetic, but the spectra are complex and insufficient is known to warrant discussion of the possible species formed. Sowden and Davidson also irradiated disulphur dichloride, but made no mention of colour.[3]

Photolysis of Ethyl Iodide.—No electron-spin resonance absorption attributable to radicals formed from ethyl iodide dissolved in ethanol was detected after irradiation for several hours. Willard and his co-workers[12] also failed to detect resonance from solid ethyl iodide after exposure to 2537 Å light, although a spectrum of six lines, attributed to ethyl radicals, was obtained after exposure to γ-radiation.

However, addition of iodine to the irradiated ethanolic solutions after warming-up resulted in the formation of tri-iodide, thus showing that iodide has been formed during photolysis. Willard and his co-workers[12] established conclusively that an important reaction during photolysis leads to the formation of ethylene and hydrogen iodide, $C_2H_5I \longrightarrow C_2H_4 + HI$, and our results suggest that this is the only important reaction occurring under our conditions.

*Photolysis of αα′-Azoiso**butyronitrile.*—This nitrile, which is used extensively as a source of free radicals in vinyl polymerisation, has a band of low intensity at 340 mμ.[13] Photolysis with 3650 Å light caused a rapid shrinking of this band and a parallel increase in a band at 2850 Å. On warming to room temperature, this new band was also destroyed. No electron-spin resonance absorption was detected at any stage. The new band is very similar to that attributed by Talat-Erban and Bywater[13] to the unstable compound $Me_2C{:}C{:}N{\cdot}C(CN)Me_2$, for which they estimated a value of 125 for the extinction coefficient. We estimate a value of 25, assuming complete conversion of the αα′-azo*iso*butyronitrile into

[10] Merz and Waters, *J.*, 1949, S15.
[11] Livingston, Ghormley, and Zeldes, *J. Chem. Phys.*, 1956, **24**, 483.
[12] Luebbe and Willard, *J. Amer. Chem. Soc.*, in the press.
[13] Talat-Erban and Bywater, *J. Amer. Chem. Soc.*, 1955, **77**, 3712.

the species absorbing at 2850 Å, so if the new compound is $Me_2C{:}C{:}N{\cdot}C(CN)Me_2$ then the reaction

$$Me_2C(CN){\cdot}N{:}N{\cdot}C(CN)Me_2 \longrightarrow N_2 + Me_2C{:}C{:}N{\cdot}C(CN)Me_2$$

contributes about one-fifth to the total decomposition.

Other possible paths, not involving radicals, are

$$Me_2C(CN){\cdot}N{:}N{\cdot}C(CN)Me_2 \longrightarrow N_2 + Me_2C(CN){\cdot}C(CN)Me_2$$

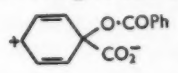
and

$$Me_2C(CN){\cdot}N{:}N{\cdot}C(CN)Me_2 \longrightarrow N_2 + Me_2CH{\cdot}CN + CH_2{:}C(CN)Me.$$

None of these products would be detected spectrophotometrically. When the nitrile was photolysed in a glass consisting largely of acrylonitrile, no polymer separated on warming. This is in contrast with the behaviour of a similar system in which the nitrile was replaced by hydrogen peroxide,[14] and the result provides further evidence for the absence of radicals.

Photolysis of Benzoyl Peroxide.—Benzoyl peroxide absorbs at 2750 Å, $\varepsilon_{max.} = 2340$. During the first few minutes of photolysis with 2537 Å light an intense yellow colour was observed. Two new bands were found at 3650 and 3050 Å and both were rapidly lost on softening. No electron-spin resonance absorption was detected. The extinction coefficient for the band at 3650 Å was found to be approximately 5600 by titrimetric estimation of the peroxide before and after irradiation. This is an upper limit if recombination can occur during warming-up.

It is possible that the unstable species is a non-radical such as the zwitterion (I), but it is also possible that the spectrum is due to benzoylperoxy-radicals which, for some reason, do not give rise to a detectable electron-spin resonance absorption. One way whereby this could occur would be for the radicals to be trapped so close together that the irradiated glass consists of isolated pairs of radicals, each sufficiently close to the other to give rise to spin–spin broadening. This could occur because of the large size and stability of benzoylperoxy-radicals. The magnetic interaction could spread out the resonance absorption beyond the limits of detection, but would not appreciably affect the ultraviolet absorption.



(I)

Absorption maxima ($\lambda_{max.}$ Å), *extinction coefficients* ($\varepsilon_{max.}$), *and electron-spin resonance results.* (*N* is the number of hyperfine lines.)

Solvent	Solute	Concn. (mol./l.)	Colour	$\lambda_{max.}$	$\varepsilon_{max.}$	*N*	
MeOH	H_2O_2	10^{-2}	Violet	5200	300	3	
EtOH	H_2O_2	10^{-2}	Violet	5200	300	5	
Pr^{n}OH	H_2O_2	10^{-2}	Violet	5200	300	5	
Pr^{i}OH	H_2O_2	10^{-2}	Violet	—	—	7	
*cyclo*Hexanol	H_2O_2	10^{-2}	Orange	4500	300	6	
tert.-Butanol	H_2O_2	10^{-2}	Colourless	—	—	3	
Diethyl ether	H_2O_2	10^{-2}	Violet	—	—	—	
Glycerol	H_2O_2	10^{-2}	Violet	—	—	1 [e]	
Ethylene glycol	H_2O_2	10^{-2}	Violet	—	—	1 [e]	
Acetic acid	H_2O_2	10^{-2}	Violet	—	—	*b*	
Formic acid	H_2O_2	10^{-2}	Violet	—	—	*b*	
Allyl alcohol	H_2O_2	10^{-2}	Yellow	—	—	4	
EtOH	$Me_2C{\cdot}O{\cdot}OH$	10^{-2}	Violet	—	—	5	
EtOH	$(Me_2CO)_2$	10^{-1}	Colourless	—	—	Nil [e]	*d*
EtOH	ClO_2	10^{-1}	Violet	—	—	*b*	
Methyl*cyclo*hexane	ClO_2	10^{-1}	Colourless	—	—	*b*	
EtOH	$(Ph{\cdot}CO_3)_2$	10^{-2}	Yellow	3650	6000	Nil [e]	*d*
Methyl*cyclo*hexane	$(Ph{\cdot}CO_3)_2$	10^{-2}	Yellow	—	—	Nil	*d*
EtOH	*c*	10^{-1}	Colourless	2850	—	Nil	
EtOH	EtI	10^{-1}	Colourless	—	—	Nil [e]	*d*
Methyl*cyclo*hexane	S_2Cl_2	10^{-1}	Red	—	—	*b*	*d*
3-Methylpentane	S_2Cl_2	10^{-1}	Blue	—	—	*b*	*d*

a = Signs of hyperfine structure. *b* = Complex spectrum. *c* = Small 5-line spectrum as found for EtOH alone. *d* = 2537 Å Radiation: otherwise 3650 Å. *e* = αα′-Azo*iso*butyronitrile.

[14] Ingram, Symons, and Townsend, *Trans. Faraday Soc.*, 1958, **54**, 409.

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Discussion

In many instances the course of photolysis in rigid media seems to differ from that in fluid media or the gas phase. Sometimes a substance which is readily photolysed in solution is not decomposed at all when the medium is rigid.[4a] We have found, in agreement with Sowden and Davidson,[4a] that prolonged irradiation of a very dilute solution of iodine does not result in loss of colour and there is no detectable electron-spin resonance absorption. This result fits in well with those of Lampe and Noyes [15] and suggests that a cage back-reaction of high efficiency is operating.

Possibly because of such back-reactions, processes which can follow both radical and non-radical paths in the fluid state seem to follow a non-radical path only in rigid media. Examples are ethyl iodide and $\alpha\alpha'$-azo*iso*butyronitrile. It is not clear whether or not radicals are transiently formed within the solvent cage before the formation of the non-radical products detected.

When radicals are trapped, they are generally found to be derived from the solvent. For example, hydroxyl radicals, which are presumably the first product in the photolysis of hydrogen peroxide, have not been detected; instead, the evidence is strong that they either extract hydrogen from the solvent or add to unsaturated compounds. The mode of interaction occurring when hydrogen peroxide is photolysed in solid acetic or formic acid is still obscure. For acetic acid, there seem to be four possibilities: (*a*) extraction of α-hydrogen to give $\cdot CH_2 \cdot CO_2H$; (*b*) attack on carboxylic hydrogen to give $CH_3 \cdot CO_2 \cdot$; (*c*) addition to give $CH_3 \cdot \overset{\displaystyle O}{\overset{|}{C}}(OH)_2$; and (*d*) addition to give $CH_3 \cdot \dot{C}(OH) \cdot O \cdot OH$.

Evidence from reactions at room temperature is ambiguous.[10,16] Also, electron-spin resonance results, although they prove conclusively the presence of trapped radicals, do not give an unambiguous identification. The appearance of a violet colour after prolonged irradiation, however, if our postulate be accepted, indicates the presence of the $\succ\dot{C}$–OH group, and hence points strongly to alternative (*d*). If addition to the carboxyl group can occur, one might expect that the direction of addition would be such as to give (*d*) rather than (*c*) since far more delocalisation of the unpaired electron is possible in (*d*), and the hydroxyl radical, being electrophilic, will tend to avoid the positively polarised carboxyl carbon. If such addition occurred at room temperature, it would probably be reversible and not detected.

Nature of the Violet Species.—This problem has been discussed,[5] and it was concluded that, in ethanol, the violet colour was due to the radical $CH_3 \cdot \dot{C}H \cdot OH$. These radicals could well have a low-energy transition involving partial charge-transfer between α-carbon and oxygen. However, some recent results [9] cast doubt on this concept so the problem requires further consideration.

All primary and secondary alcohols so far studied become violet after photolysis of dilute solid solutions of hydrogen peroxide, or have a broad band in the 500 mμ region. Tertiary alchols do not develop a band in this region. Irradiation of *tert.*-butyl hydroperoxide or chlorine dioxide in ethanol gives the same colour, but no colour develops when either is irradiated in a mixed hydrocarbon glass. Thus primary or secondary alcohols seem to be necessary ingredients.

Evidence is presented in Part II [17] that primary and secondary alcohols lose α-hydrogen under these conditions. If this is correct, then only when the unit $\succ\dot{C}$–OH is present is a band in the 500 mμ region found.

Alger *et al.*[9] have observed similar colours after high-energy irradiation of solid alcohols. There is one remarkable difference, however: alcohol glasses so coloured are readily

[15] Lampe and Noyes, *J. Amer. Chem. Soc.*, 1954, **76**, 2140.
[16] Koltoff and Medalia, *ibid.*, 1949, **71**, 3777.
[17] Part II, following paper.

bleached by visible light whereas our glasses are unaffected. Alger *et al.*[9] obtained very similar electron-spin resonance spectra to ours, and observed no change in these spectra after photo-bleaching. They therefore concluded that the coloured species are *not* the free radicals which give rise to the resonance absorption. The reason for this surprising difference is not understood.

One alternative explanation is that colour-centres are formed, similar to *F*-centres found in ionic crystals. Photolysis of triphenylmethyl-lithium in an E.P.A. glass (*i.e.*, one made from diethyl ether, *iso*pentane, and ethanol) results in photoionisation, but no discrete absorption due to unpaired electrons appeared in the visible region of the spectrum.[4b] Again, our experiments with solutions saturated with lithium chloride strongly suggest that trapped electrons are not the cause of colour, since lithium ions would surely provide good traps for ejected electrons and as a result new colour centres would be formed.

Alternatively, the colour might be due to radical-positive ions remaining after loss of electrons. Such a postulate is reasonable when high-energy radiation is employed, but photo-ionisation is unlikely to be induced by light of 3650 Å wavelength.

We thank Dr. C. H. Bamford and Dr. A. Jenkins for helpful discussion. For this and the following paper we thank Dr. D. J. E. Ingram for help relating to electron-spin resonance measurements, and Courtaulds Ltd. for a grant (to M. G. T.).

DEPARTMENT OF CHEMISTRY, THE UNIVERSITY, SOUTHAMPTON. [*Received, June 16th*, 1958.]

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47. *Unstable Intermediates. Part II.*[1] *Photolysis of Hydrogen Peroxide in Solid Alcohols: Some Reactions of Hydroxyl Radicals.*

By J. F. GIBSON, M. C. R. SYMONS, and M. G. TOWNSEND.

When hydrogen peroxide, in dilute solution in alcohols at 77° K, is photolysed, characteristic changes in the visible and ultraviolet spectra are accompanied by intense electron-spin resonance signals containing marked hyperfine structure. Previous results [1,2] have been extended by varying the irradiation conditions and the choice of solvent. In particular, the electron-spin resonance spectra recorded during the initial stages of photolysis and during warming-up are discussed. The hyperfine patterns, attributed to radicals derived from alcohols, can be interpreted in terms of α-hydrogen abstraction in certain cases. Possible explanations for the other spectra are presented and discussed in terms of the known reactivity of hydroxyl radicals.

PHOTOLYSIS [1,2,3] of dilute solid solutions of hydrogen peroxide by 3650 Å light is a general method for producing trapped radicals which can then be studied in detail by ultraviolet and electron-spin resonance spectroscopy. The trapped radicals always arise through loss of hydrogen by the solvent or addition of hydroxyl radicals to double bonds. Results of those previous experiments are now summarised, and new results obtained from a wide range of saturated aliphatic alcohols are reported. The results are tabulated, and representative spectra reproduced in the Figures. During the initial stages of photolysis, except for very dilute solutions, a single line with a shoulder at low field strength is observed (Stage I). After a few minutes another spectrum appears, and after prolonged irradiation, this completely masks the former (Stage II). This new spectrum invariably contains considerable hyperfine structure. Finally, when the temperature of the glass is allowed to approach the softening point, the Stage II spectrum is lost, and two alternative spectra are observed (Stage III). Sometimes an asymmetric line similar to that at Stage I is recorded, and at others a single, relatively narrow symmetrical line is found. Further

[1] Part I, Symons and Townsend, preceding paper.
[2] Gibson, Ingram, Symons, and Townsend, *Trans. Faraday Soc.*, 1957, **53**, 914.
[3] Ingram, Symons, and Townsend, *ibid.*, 1958, **54**, 409.

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increase in temperature results in complete loss of signal. These changes, which are independent of the alcohol, are summarised in the Figures. A further complication appeared; the general appearance of the Stage II spectra seems to depend on the conditions, and at times the relatively simple spectra recorded earlier [2] are found to be considerably more complicated (see Fig. 4).

The experimental procedures were as previously described.[1] For some experiments a resonance cavity constructed for irradiation *in situ* was employed [4] which gave results identical with those obtained by periodically transferring the specimen from a Dewar flask containing liquid nitrogen into the cooled cavity.

Fujimoto and Ingram [4] repeated many of these experiments and largely confirmed our results. The few differences which do occur will be commented on as appropriate. Their interpretations, which are quite different from ours, will be discussed in Part III.[5]

Results and Discussion

The results are presented in the Table and Figures and will be discussed in the following order:

(i) *Nature of the Changes occurring during Initial Photolysis, and Thermally after Photolysis* (*Stages* I—III).—Alcoholic solutions which are 0·1M or stronger in hydrogen peroxide will probably contain some clusters of hydrogen peroxide molecules. Such clusters will be increasingly important as the length of the hydrocarbon chain increases. On photolysis, such units would probably decompose according to the sequence

$$H_2O_2 + h\nu \longrightarrow 2{\cdot}OH$$
$$\cdot OH + H_2O_2 \longrightarrow H_2O + HO_2\cdot$$

thus giving rise to $HO_2\cdot$ radicals. This is likely to occur more readily than the main reaction of hydrogen abstraction from the solvent, and since, at the temperatures employed, $HO_2\cdot$ radicals would not attack the solvent, the first radicals to be detected by electron-spin resonance would be $HO_2\cdot$. When such units are consumed, the major reaction becomes abstraction, by hydroxyl, of that hydrogen atom in the solvent molecule most susceptible to attack and, superimposed upon the small signal from $HO_2\cdot$ radicals (Stage I), the spectrum of the solvent radicals will appear (Stage II).

If, subsequently, the glass is allowed to soften sufficiently to permit migration of the solvent radicals (R·), then more $HO_2\cdot$ radicals would be formed, provided some hydrogen peroxide remains, and the single asymmetric line could again predominate:

$$R\cdot + H_2O_2 \longrightarrow RH + HO_2\cdot$$

If the warming-up is allowed to continue then oxygen formed during reaction, and any oxygen originally present, would also be liable to interact with all radicals:

$$R\cdot + O_2 \longrightarrow RO_2\cdot$$
and $$HO_2\cdot + O_2 \longrightarrow HO_4\cdot$$
or $$\cdot OH + O_2 \longrightarrow HO_3\cdot$$

In the absence of excess of hydrogen peroxide, reaction with oxygen would be the only reaction likely to result in the formation of a different radical species (Stage III).

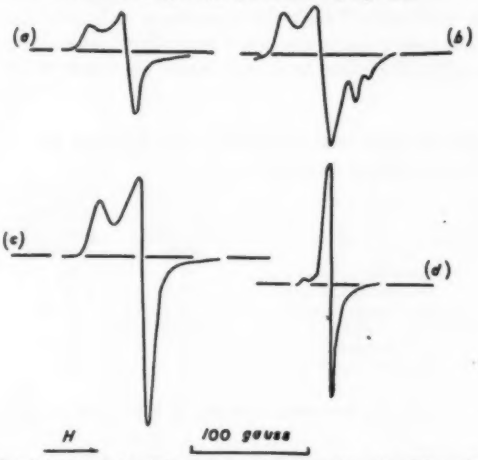
If these considerations concerning possible radical species are correct, then the electron-spin resonance spectra shown in Figs. 1*a* and 2*a* must be attributed to the $HO_2\cdot$ radical. The shape of this line is characteristic of radicals having a variation in g-value with orientation in the magnetic field. This means that the orbital containing the unpaired electron has axial symmetry. If the peak at $g = 2{\cdot}004$ is attributed to that extreme in which radicals are perpendicular to the field ($g_\perp$), then the shoulder at $g = 2{\cdot}024$ is due to radicals lying parallel with the field ($g_\parallel$). These values for $g_\parallel$ and $g_\perp$ may be compared

[4] Fujimoto and Ingram, *Trans. Faraday Soc.*, 1958, **54**, 1304.

with those obtained by Livingston *et al.*,[5] and attributed to $HO_2^{\bullet}$, namely, $g_{\perp} = 2{\cdot}008$ and $g_{\parallel} = 2{\cdot}027$. The spread is almost identical and the slight difference in absolute value is probably within experimental error.

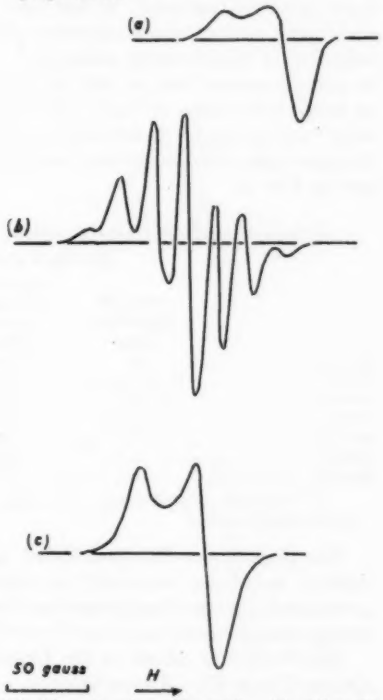
It is noteworthy that Livingston *et al.*[5] observed a yellow colour in solids thought to contain $HO_2^{\bullet}$. We found that when a purple alcohol glass containing a large excess of hydrogen peroxide is allowed to warm under controlled conditions, the violet changes to yellow before complete loss of colour.[1]

FIG. 1. *Electron-spin resonance spectra from photolysed solutions of hydrogen peroxide in propanol.*



(*a*) After 3 min. (Stage I). (*b*) After 15 min. (Stage I and Stage II). (*c*) After partial softening and refreezing (*b*) (Stage III). (*d*) After further warming and refreezing (*c*) (Stage III).

FIG. 2. *Electron-spin resonance spectra from photolysed solutions of hydrogen peroxide in propan-2-ol.*



(*a*) After 5 min. (Stage I). (*b*) After 30 min. (Stage II). (*c*) After partial softening and refreezing (*b*) (Stage III).

Further support for the postulate that the asymmetric line is caused by $HO_2^{\bullet}$ comes from the fact that when alcohols are irradiated with *X*-rays or high-energy electrons, electron-spin resonance and ultraviolet spectra are recorded which are generally very similar to those recorded here (Stage II) but an asymmetric single line has never been detected in these studies. Thus, hydrogen peroxide is an essential ingredient.

Comparison of the spectrum attributed to $HO_2^{\bullet}$ with that found for its conjugate base, O_2^{-}, shows that these lines are very similar in form, but that the variation in *g*-value is very much greater in the case of superoxide.[6] For superoxide in the absence of asymmetric electric fields one would predict $g_{\parallel} = 4$ and $g_{\perp} = 0$, and the experimental values of $g_{\parallel} = 2{\cdot}175$ and $g_{\perp} = 2{\cdot}002$ show that strong asymmetric fields lift the degeneracy of the

[5] Livingston, Ghormley, and Zeldes, *J. Chem. Phys.*, 1956, **24**, 483.
[6] Bennett, Ingram, Symons, George, and Griffith, *Phil. Mag.*, 1955, **46**, 443.

π orbitals, thus quenching spin–orbit coupling. In $HO_2^{\bullet}$, the strong field of the proton splits the levels to an even greater extent, and hence the observed *g*-values are reasonable.

Little can be said about the nature of the single symmetric line often observed during warming-up. The ozonide ion, O_3^-, shows little or no variation in *g*-value, but the line is broad and the *g*-value of 2·012 is quite far from the average value of 2·004 found for alcohol radicals.[7] Further loss of symmetry would decrease spin–orbit coupling still further and therefore there seems no inconsistency in this sense, with the theory outlined above, that the single line is caused by addition of oxygen, and indeed, this postulate has often been made in other contexts. It has been suggested that this single line is to be associated with some sort of charge-transfer process whereby an electron passes from an alcohol radical to a neighbouring molecule.[4] It is not clear why such a process should give rise to a single narrow line, or why the transfer should occur when the solvent molecules have no low-lying vacant orbital. The further conclusion [4] that this process is only effective at 90° and not at 77° is not confirmed by our results since the specimen which gave rise to the spectrum recorded in Fig. 1*d* gave exactly the same spectrum when recorded at 77° and at 110° K.

Details of electron-spin resonance spectra obtained from irradiated solid solutions of hydrogen peroxide in various alcohols.

	No. of hyperfine lines	Hyperfine splitting constant (gauss)		No. of hyperfine lines	Hyperfine splitting constant (gauss)
MeOH	3	19	Bu^{t}OH	3	24
EtOH	5 (10, *a*, *c*)	22	*n*-Pentyl alcohol	7, *c*	20
Pr^{n}OH	5 (6, *b*)	22	*iso*Pentyl alcohol	7, 4, *c*	21, 21
Pr^{i}OH	7 (6, *a*)	20	*tert.*-Amyl alcohol	5, *c*	25
Bu^{n}OH	7, *c*	20	Allyl alcohol	4	13
Bu^{i}OH	8, *c*	23	*cyclo*Hexanol	6	20
Bu^{s}OH	6	21			

a = Occasionally observed. *b* = Ref. 4. *c* = Poorly resolved, therefore H.F.S. constant is an approximate value.

The phenomena discussed above, and illustrated in Figs. 1 and 2 for *n*- and *iso*-propyl alcohol, were also observed for other alcohols and seem to be quite general. The asymmetric line previously reported for ethanol [2] was a consequence of partial warming-up during measurement and is now attributed to $HO_2^{\bullet}$.

(ii) *Position of Attack on the Alcohol Molecule as inferred from Electron-spin Resonance Spectra* (*Stage* II).—Unfortunately, in only a few cases can the Stage II electron spin resonance spectra be interpreted with some certainty. One might have expected that this technique would have given quite unambiguous results, as is often the case for complex aromatic radicals and radical ions in solution. This is not so, largely because rigid glasses have to be used, and hence dipolar interactions are considerable and give rise to broad lines. In mobile solution, these effects are averaged to zero, leaving only the isotropic interaction, which results in very narrow lines. This severe limitation means that with lines about 15 gauss wide at half-height and with hyperfine splitting constants of the order of 20 gauss, resolution is very poor, and small differences between different hydrogen atoms cannot be detected.

We have suggested [2] that the observed hyperfine patterns arise through interactions between unpaired electrons and the nuclei of α- or β-hydrogen atoms. This α–β rule will be assumed throughout this discussion and an attempt will be made to justify this assumption in Part III.[8]

The simplicity and apparent symmetry of derivative spectra can often be deceptive. For example, the spectrum recorded for the anthracene positive ion [9] contains 19 or 21

[7] McLachlan, Symons, and Townsend, *J.*, in the press.
[8] Part III, following paper.
[9] Weissman, de Boer, and Conradi, *J. Chem. Phys.*, 1957, **26**, 963.

lines with apparently equal spacing for all lines. However, better resolution has shown that this is fortuitous, the new spectrum containing about 50 lines which are by no means evenly distributed.[10] All that can be done is to assume that the spectra are as simple as they appear, but this assumption may be far from the truth.

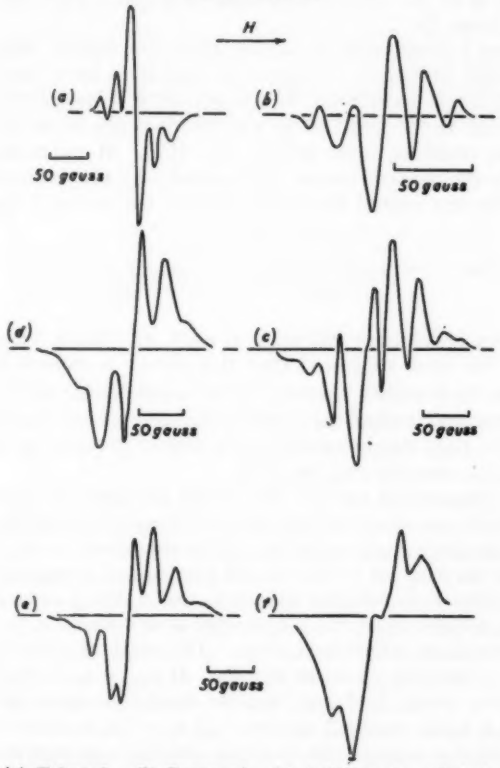
Methanol, ethanol, and propan-2-ol present reasonably well-resolved spectra of **3**, **5**, and **7** lines having an approximately gaussian distribution of intensities. The hyperfine splitting constants of 19, 22, and 20 are quite in accord with the postulate that α-hydrogen is removed in each case, giving, respectively, $\cdot CH_2 \cdot OH$, $CH_3 \cdot \dot{C}H \cdot OH$, and $(CH_3)_2\dot{C} \cdot OH$.[2,8]

tert.-Butyl alcohol and *tert.*-amyl alcohol give 3 and 5 lines, and it is postulated that the predominating radicals are respectively $\dot{C}H_2 \cdot CMe_2 \cdot OH$ and $CH_3 \cdot \dot{C}H \cdot CMe_2 \cdot OH$.

From these conclusions one can deduce that α-hydrogen atoms are abstracted in preference to primary β-hydrogen atoms, and that in the absence of the former, secondary are abstracted in preference to primary hydrogen atoms.

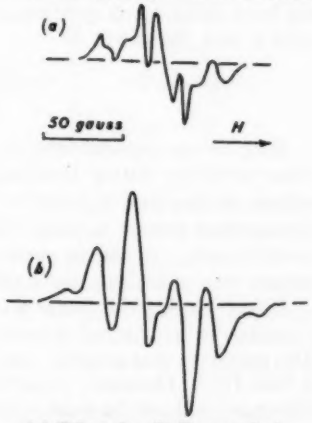
From this stage onwards, however, interpretation of electron-spin resonance spectra is somewhat arbitrary. This can be illustrated by a consideration of the spectrum from propan-1-ol. We reported earlier an unsymmetrical five-line spectrum.[2] Further study

FIG. 3. *Electron-spin resonance spectra attributed to alcohol radicals.*



(*a*) Ethanol. (*b*) Propanol. (*c*) *iso*Butanol. (*d*) *tert.*-Amyl alcohol. (*e*) *iso*Pentyl alcohol. (*f*) *iso*Pentyl alcohol.

FIG. 4. *Alternative electron-spin resonance spectra for alcohol radicals.*



(*a*) Ethanol. (*b*) Propan-2-ol.

[10] Carrington and Symons, *J.*, in the press.

has enabled us to obtain a quintet of far greater symmetry (Fig. 3*b*). Integration of this derivative shows that the line-intensity ratios are close to binomial distribution and that the hyperfine splitting constant is about 22. We suggested that the 5-line spectrum was built from a single central line and a symmetrical quartet. The better resolution and greater symmetry of the spectrum (Fig. 3*b*) render this interpretation untenable. Alger, Anderson, and Webb [11] obtained a spectrum very similar to ours after bombarding solid propan-1-ol with *X*-rays or high-energy electrons. These spectra were reproducible and were quite similar when observed at 77° or 90° K. The spectrum shown in Fig. 1*b* represents a halfway stage between Stage I and Stage II.

In contrast, Fujimoto and Ingram [4] found that a six-line spectrum results when hydrogen peroxide is photolysed in rigid propanol, sometimes accompanied by a single line. The reason for these differences is not understood, so interpretation is speculative.

The most obvious parameter to vary is the point of attack, which could be on the α-, β-, γ-, or hydroxyl-hydrogen atoms, resulting in the radicals (I)—(IV). If one makes the simplifying assumption, justified in the case of ethanol, that α- and β-hydrogen atoms will have about equal splitting, then the first radical should give 4 lines, the second 7, the third 5, and the fourth 3.

$CH_3{\cdot}CH_2{\cdot}\dot{C}H{\cdot}OH$ (I) $\quad$ $CH_2{\cdot}\dot{C}H{\cdot}CH_2{\cdot}OH$ (II) $\quad$ $\dot{C}H_2{\cdot}CH_2{\cdot}CH_2{\cdot}OH$ (III) $\quad$ $CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}O{\cdot}$ (IV)

Both in our experiments, and when high-energy radiation is used, an intense violet colour develops during irradiation. We have suggested that this colour is caused by radicals of structure $R_2\dot{C}{\cdot}OH$.[1] If this be accepted, then one must conclude that radical (I) is present at least in part. However, only radical (III) seems to fit in with the experimental result. It will be shown below that this is unlikely on chemical grounds, so at present we can find no reasonable explanation for this spectrum.

Before leaving the problem of the propan-1-ol radical, one should consider the types of spectra to be expected if α- and β-hydrogen atoms do not give nearly equal interaction. (The postulate that roughly equal interaction is to be expected will be considered in detail in Part III.[8] However, inspection of the data for methanol and propan-2-ol shows that differences will not be great and certainly one would not expect to find a factor as large as 2 involved.) For radical (I), it is possible that the β-hydrogen atoms would give a slightly different splitting from the remaining α-hydrogen atom. This state of affairs is illustrated in Fig. 5. When $a_1 = a_2$, a four-line spectrum results. If $a_1 > a_2$ a sextet (1 : 1 : 2 : 2 : 1 : 1) with unequal spacing would be found, but for small differences and broad lines, this would still appear as a badly resolved quartet. If $a_1 = 2a_2$ a sextet of equally spaced lines would be found, but this extreme difference has already been rejected. Again, if $a_2 = 2a_1$ a symmetrical quintet (1 : 2 : 2 : 2 : 1) would result, but this extreme is equally unlikely.

The difficulty encountered with propan-1-ol is also met with in the case of the higher normal primary alcohols. Thus for *n*-butanol, our spectrum appears to be either a 6- or a 7-line pattern with a strong central line superimposed. Alger *et al.*[11] obtained a 7-line spectrum, poorly resolved but apparently symmetrical, and Fujimoto and Ingram reported a 6-line spectrum.[4] We cannot offer any simple explanation of these spectra.

The *iso*-primary alcohols give patterns which are more susceptible to interpretation. The most probable points of attack are now the α- and the tertiary hydrogen atoms. For *iso*butanol the two radicals to be expected are $(CH_3)_2CH{\cdot}\dot{C}H{\cdot}OH$ and $(CH_3)_2\dot{C}{\cdot}CH_2OH$, which should give rise to 3 or 9 lines respectively, if all α- and β-hydrogen atoms are nearly equivalent. The spectrum (Fig. 3*c*) consists of eight poorly resolved lines. Accordingly, we postulate that the tertiary hydrogen atom has been attacked preferentially, but that for some reason, one of the eight β-hydrogen atoms is not interacting with the unpaired electron.

[11] Alger, Anderson, and Webb, in the press.

It is interesting to compare this result with that of Alger *et al.*[11] who find a well-defined triplet, very similar to that obtained from methanol. It would seem reasonable to postulate that loss of α-hydrogen has occurred under these conditions.

In contrast, the spectrum obtained from *iso*pentyl alcohol after exposure to high-energy radiation[11] consists of 9 lines, which points strongly to the radical $(CH_3)_2\dot{C}\cdot CH_2\cdot CH_2\cdot OH$. Our spectrum of 7 lines (Fig. 3*e*) could well be part of the same 9-line pattern, since the intensity of the outermost lines in a 9-line spectrum from eight equivalent hydrogen atoms will only be 1/70th of that of the central line and could easily be lost in background noise. However, under some conditions the spectrum appears to be a very poorly resolved quartet (Fig. 3*f*), which is what one would expect for the radical $(CH_3)_2CH\cdot CH_2\cdot\dot{C}H\cdot OH$ resulting from attack on α-hydrogen. We are not certain yet what precise conditions are required to give these alternative spectra.

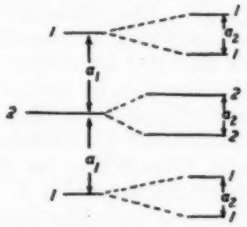


FIG. 5. *Hyperfine structure expected from two equivalent protons* (hyperfine splitting constant = a_1) *and one other proton* (hyperfine splitting constant = a_2).

sec.-Butyl alcohol gave a very poorly resolved sextet with a hyperfine splitting constant of about 22 gauss. It is tempting to assign the structure $CH_3\cdot CH_2\cdot\dot{C}Me\cdot OH$ to this radical, but the radical $CH_3\cdot\dot{C}H\cdot CHMe\cdot OH$ would also be expected to give six lines.

The spectra recorded in Fig. 4*a* and *b* are reproduced here to illustrate the fact that reproducibility is not as good as one would wish. As yet, we have found no systematic trends in variation of environment which will account for these differences. Occasionally some fault in instrumentation may cause these phenomena but if this is so, it has as yet escaped detection.

If the differences observed reflect real differences in the trapped radicals then there are two alternative explanations. One is that slight differences in environment can give rise to modifications in the interactions between protons and unpaired electrons in a given type of radical, and the other, that slight differences in experimental procedure can result in the formation of different radical species.

We do not yet propose to discuss the former explanation. The latter appears improbable on chemical grounds, but so little is known about reactions under these conditions that it ought to be considered. The spectrum obtained from ethanol (Fig. 4*a*) can be built up from two 5-line spectra having hyperfine-splitting constants of 22 and 25 gauss. The normal 5-line spectrum thought to be caused by $CH_3\cdot\dot{C}H\cdot OH$ radicals has a constant of 22 gauss: the other spectrum could then arise from the radical $\dot{C}H_2\cdot CH_2\cdot OH$.

Similarly the unusual propan-2-ol spectrum (Fig. 4*b*) can be obtained by superimposing a set of 4-lines having a hyperfine-splitting constant of 27 gauss upon the usual 7-line spectrum. This could be caused by $\dot{C}H_2\cdot CHMe\cdot OH$ radicals. We conclude that, if a considerable amount of β-attack occurred, one might well obtain spectra such as those in Fig. 4*a* and *b*. There are doubtless many other possible explanations, but if this interpretation were correct, one is at once faced with the difficult problem of understanding why attack is selective at one time and non-selective at others.

(iii) *General Observations on the Activity of Hydroxyl Radicals.*—In view of the preceding discussion it is advisable to turn to some other criterion to obtain information about the radicals resulting from attack by hydroxyl radicals on alcohols. Accordingly, the behaviour of hydroxyl radicals with respect to attack on hydrogen is briefly reviewed.

Important amongst the factors influencing relative rates of attack by radicals on various hydrogen atoms in a molecule are the stability of the displaced radical, the degree of bond breaking in the transition state, and the electrophilic or nucleophilic nature of the radical. The discrimination observed will also be a function of the temperature, increasing generally as the temperature is lowered.

The stability of the displaced radical will be important only if a considerable degree of C–H bond breaking has occurred before the transition state is reached. Comparison of the behaviour of methyl radicals on the one hand and chlorine atoms on the other has led to the conclusion [12] that only in the former case is the degree of bond breaking extensive. That means that when chlorine atoms attack hydrogen, the stability of the displaced radical is unimportant, and the overriding directive influence is the inductive effect of substituents. Chlorine atoms, with a high electron affinity, seek electron-rich centres and therefore selectively avoid α- and, to a less extent, β-hydrogen atoms in alkyl halides and carboxylic acids. The reverse is true for methyl radicals.

Hydroxyl radicals lie between these two extremes. Their electron-affinity is considerably smaller than that for chlorine atoms, whilst the proton affinity of hydroxide ions is much smaller than that for methyl negative ions.

The hydroxyl group in alcohols has a far weaker inductive effect than either chlorine or carboxyl and hence the tendency for electrophilic radicals to avoid α-hydrogen atoms will be less for alcohols than for alkyl halides or carboxylic acids.

All experimental data point to the conclusion that free radicals, whatever their nature, attack primary and secondary alcohols and ethers on α-hydrogen. Little is known about the reactions which occur between hydroxyl radicals and alcohols at room temperature, but, if one accepts the postulate that Fenton's reagent reacts as a source of hydroxyl radicals, then this reagent's reacting with propanol to give propionaldehyde establishes that α-attack is significant.[13] However, *tert.*-butylperoxy- and benzoylperoxy-radicals probably resemble hydroxyl radicals fairly closely, and both these reagents attack alcohols and ethers readily on α-hydrogen.[14,15] In the absence of α-hydrogen atoms, reaction is much slower.[14] (The conclusion that, in the absence of α-hydrogen, hydroxyl radicals attack hydroxyl-hydrogen [13] is not upheld by our results, which establish conclusively that, under our conditions, attack on β-hydrogen predominates.)

We conclude on chemical grounds that attack by hydroxyl radicals on primary and secondary alcohols will occur on α-hydrogen. If this is correct, then the uninterpreted electron-spin resonance spectra recorded must be due to radicals of type $R_2\dot{C}\cdot OH$ and there is some factor, so far overlooked, which would make this conclusion intelligible. The same conclusion was reached in Part I on spectroscopic grounds.[1]

When a tertiary hydrogen atom is present in the alkyl group as in the *iso*-primary alcohols, attack on this atom would be more favoured than on other primary or secondary hydrogen atoms because the C–H bond strength is relatively small and the displaced radical is greatly stabilised by the two methyl groups. Our results suggest that there is a rather fine balance between α-attack and attack on tertiary hydrogen: if this is correct, then one can again conclude that α-attack will predominate in the absence of tertiary hydrogen. These results can be compared with those of Kenyon and Symons who concluded that hydroxyl radicals attacked the anions of branched-chain carboxylic acids preferentially on tertiary hydrogen.[16]

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DEPARTMENT OF CHEMISTRY, THE UNIVERSITY, SOUTHAMPTON. [*Received, June 16th*, 1958.]

[12] Russell and Brown, *J. Amer. Chem. Soc.*, 1955, **77**, 4578.
[13] Merz and Waters, *J.*, 1949, 2427.
[14] Bartlett and Nazaki, *J. Amer. Chem. Soc.*, 1947, **69**, 2299.
[15] Urry, Stacey, Huyser, and Juveland, *ibid.*, 1953, **75**, 250; 1954, **76**, 450.
[16] Kenyon and Symons, *J.*, 1953, 3580.

48. *Unstable Intermediates. Part III.*[1] *Proton Interaction in Aliphatic Free Radicals.*

By M. C. R. Symons.

Values of hyperfine splitting constants obtained from electron-spin resonance spectra of aliphatic free radicals are correlated on the basis of certain simplifying assumptions. When radicals have been identified with reasonable certainty, good agreement is obtained: in other cases the observed splitting is of value for identification.

Interaction between unpaired electrons and β-hydrogen atoms is a function of the angle between the plane of the C–H bond and the nodal plane of the unpaired electron, and, if rotation is restricted, β-hydrogen atoms may cease to be equivalent. A variety of results is considered in terms of this principle.

An explanation is offered of the fact that, often, completely different reactions result in the final trapping of the same radicals. Some outstanding anomalies are discussed.

Although considerable attention has been given to the quantitative features of electron-spin resonance spectra obtained from stable aromatic radicals and radical ions, very little has been paid to the spectra of simple aliphatic free radicals. One reason for this is that the spectra of simple radicals trapped in solids are often difficult to interpret.[1] Indeed, since it is often not known what radicals have been trapped, the problem of interpretation becomes dependent upon identification, which may also be difficult.[1]

Despite these difficulties, it is felt that many recent results can be correlated fairly accurately, provided some simplifying assumptions are made. The procedure rests upon the basic assumption that simple radicals such as $\cdot CH_3$, $CH_3 \cdot CH_2 \cdot$, $\cdot CH_2 \cdot OH$, etc., have been trapped, and that the spectra do, in fact, relate to these radicals. This identification is rarely compelling but is generally reasonable, and will be accepted provisionally in order that certain quantitative aspects of these spectra may be examined.

The assumptions and calculations relating to hyperfine splitting constants are presented in Section I and the results compared with experimental values in Tables 2, 3, and 4. These results are then discussed. In Section II some aspects of hyperconjugation are considered, especially with regard to hindered rotation. In Section III some general remarks are made concerning outstanding anomalies in the field of radical-trapping.

I. *Symbols.*—a is the hyperfine splitting constant, *i.e.*, the separation (gauss) between hyperfine lines in the electron-spin resonance spectra; $a_{\alpha H}$ and $a_{\beta H}$ are its values for α- (as in $\cdot CH_3$) and β-hydrogen atoms (as in $\cdot CMe_3$), and a_{av} is the average of, and Δa the difference between, them. ρ_C is the unpaired electron density on trigonally-hybridised carbon (%); $X_{\alpha H} = a_{\alpha H}/\rho_C$ and $X_{\beta H} = a_{\beta H}/\rho_C$; $A_{\alpha H}$ and $A_{\beta H}$ are the delocalising powers of α- or β-hydrogen atoms; $\rho_C \cdot A_{\alpha H}$ is the unpaired electron density on each α-hydrogen atom; A_y is the delocalising power of Y as in $\cdot CH_2Y$; $\theta = 90°$ minus the angle between a β-C–H bond and the nodal plane of the unpaired electron.

Assumptions and Calculations.—It is first assumed that the hyperfine splitting constant is a measure of the unpaired electron density on hydrogen. The experimental value for hydrogen atoms is 502 gauss. If, then, a particular hydrogen atom gives a splitting of a gauss, the unpaired electron density on this hydrogen atom will be $a/5{\cdot}02\%$.[2]

The second assumption is that both $a_{\alpha H}$ and $a_{\beta H}$ will be linearly proportional to ρ_C. This is equivalent to McConnell's equation $a_N = Q\rho_n$ for aromatic radicals,[3] but represents a considerable and, as yet, unjustified extension to cases when ρ is large and both α- and β-hydrogen atoms interact with the unpaired electron.

[1] Gibson, Symons, and Townsend, preceding paper.
[2] Gibson, Ingram, Symons, and Townsend, *Trans. Faraday Soc.*, 1957, **53**, 914.
[3] McConnell, *Ann. Rev. Phys. Chem.*, 1957, **8**, 116.

TABLE 1. *Alternative values for factors $A_{\alpha H}$, $A_{\beta H}$, $X_{\alpha H}$, and $X_{\beta H}$, derived from electron spin resonance spectra of methyl and* tert.*-butyl radicals.*[4]

Radical	Procedure	$A_{\alpha H}$	$X_{\alpha H}$	$A_{\beta H}$	$X_{\beta H}$
$\cdot CH_3$	(i)	0	0·26	—	—
	(ii)	0·062	0·31	—	—
	(iii)	−0·045	0·226	—	—
$\cdot CMe_3$	—	—	—	0·078	0·393

TABLE 2. *Estimated and experimental values of hyperfine splitting constants for the radicals* $\cdot CH_2Me$ *and* $\cdot CHMe_2$ [*by use of procedures* (i), (ii), *and* (iii) *outlined above*].

Radical	ρ_C (%)	$a_{\alpha H}$	$a_{\beta H}$	a_{av} (est.)	a_{av} (exp.)	Δa (est.)	Δa (exp.)
$\cdot CH_2Me$	(i) 81	21	31·8	27·5	26,[6] 24 [4]	10·8	6 [4]
	(ii) 73·6	22·8	28·8	26·4	—	6·0	Not resolved [6]
	(iii) 87·4	19·8	34·3	28·5	—	14·5	
$\cdot CHMe_2$	(i) 68·2	17·7	26·7	25·4	25·0 [4]	9·0	Not resolved [4]
	(ii) 65·4	20·3	25·7	25·0	—	5·4	
	(iii) 70·3	15·8	27·6	26·0	—	11·8	

TABLE 3. *Estimated and experimental values of hyperfine splitting constants for various radicals from alcohols.*

No.	Radical	ρ_C	$a_{\alpha H}$	$a_{\beta H}$	a_{av}	a_{exp} [1]	Δa (est.)	N (est.)	N [1] (exp.)
1	$\cdot CH_2\cdot OH$	61·3	(19)	—	—	19	—	3	3[a]
2	$CH_2\cdot\dot{C}H\cdot OH$	55·7	17·3	21·9	20·8	21	4·6	5	5
3	$\cdot CH_2\cdot CH_2\cdot OH$	75	23·3	29·5	26·4	25	6·2	5	5[b]
4	$\cdot CMe_2\cdot OH$	50·8	—	20	—	20	—	7	7
5	$\cdot CH_2\cdot CHMe\cdot OH$	76·5	23·7	30·2	26	27	6·5	4	4[b]
6	$CH_2\cdot CH_2\cdot\dot{C}H\cdot OH$	56·5	17·6	22·2	20·8	22	4·6	4	5
7	$CH_2\cdot\dot{C}H\cdot CH_2\cdot OH$	71·2	22·1	28	27	22	6·1	7	5
8	$\cdot CH_2\cdot CH_2\cdot CH_2\cdot OH$	75	23·3	29·5	26·4	22	6·2	5	5
9	$Me_2\dot{C}\cdot CH_2\cdot OH$	59·7	—	23·4	—	23	—	9	8
10	$Me\dot{C}(OH)Et$	53	—	21	—	21	—	6	6
11	$Me\dot{C}H\cdot CH(OH)Me$	67·6	21	26·6	25·5	21	5·6	6	6
12	$\cdot CH_2\cdot CMe_2\cdot OH$	77·5	(24)	—	—	24	—	3	3[a]
13	$CH_2\cdot\dot{C}H\cdot CMe_2\cdot OH$	68·7	21·5	27	25·5	25	5·5	5	5

[a] Value assumed. [b] Experimental results may well be spurious.[1] N = No. of hyperfine lines.

TABLE 4. *Estimated values for* A_Y *in radicals* $R_2\dot{C}$–Y.

Y	OH	O^-	CN	CO_2Me	$CO\cdot NH_2$	$CMe_2\cdot OH$	CH_3
A_Y	0·5	0·8	0·75	0·52	0·26	0·16	0·234

Accepting these postulates, we make the calculations as follows: From the value $a = 26$ for $\cdot CH_3$ [4] a figure for $A_{\alpha H}$ is estimated. Three alternative approaches can be made. (i) That $\rho_C = 100$, that is, that α-hydrogen effects no delocalisation, and therefore that $A_{\alpha H} = 0$ and $X_{\alpha H} = 0{\cdot}26$. (ii) That α-hydrogen atoms effect a delocalisation, measured by the value of 26 gauss for a. On this basis, the unpaired electron density is 26/5·02% on each hydrogen atom, or 15·55% on all three. That means $\rho_C = 84{\cdot}45$ and hence $A_{\alpha H} = 0{\cdot}062$ and $X_{\alpha H} = 0{\cdot}31$. (iii). In view of the postulate that positive spin on carbon gives rise to negative spin on α-hydrogen atoms, (ii) may be false, and it might be more correct to say that the spin on α-hydrogen atoms is −15·55, and hence that ρ_C = 115·55%. On this basis, $A_{\alpha H} = -0{\cdot}045$ and $X_{\alpha H} = 0{\cdot}226$.

From the value $a = 23$ for $\cdot CMe_3$,[4] and the assumption that positive spin on carbon gives rise to positive spin on β-hydrogen atoms, the unpaired electron density is 23/5·02% on each β-hydrogen or 41·3% on all nine β-hydrogen atoms. Hence, $\rho_C = 58{\cdot}7$, $A_{\beta H}$ = 0·078, and $a_{\beta H} = 0{\cdot}393$. These results can now be used to estimate $a_{\alpha H}$ and $a_{\beta H}$ in the radicals $\dot{C}H_2Me$ and $\dot{C}HMe_2$. For $\dot{C}H_2Me$ the total unpaired electron density of 100% can

[4] Matheson and Smaller, *J. Chem. Phys.*, 1958, **28**, 1169.

be equated to the amount on carbon, ρ_C, that on α-hydrogens, $2A_{\alpha H}\rho_C$, and that on methyl, $3A_{\beta H}\rho_C$: *i.e.*, $100 = \rho_C + 2A_{\alpha H}\rho_C + 3A_{\beta H}\rho_C$, whence $\rho_C = 81$, 73·6, or 87·4% for procedures (i), (ii), and (iii) respectively. From these values for ρ_C, $a_{\alpha H}$, and $a_{\beta H}$ have been calculated and are given in Table 2 together with values for a_{av} and Δa.

Similarly, ρ_C for the radical ·$CHMe_2$ can be calculated from the equation $100 = \rho_C + A_{\alpha H}\rho_C + 6A_{\beta H}\rho_C$. The results obtained again depend upon the procedure used, as do the estimates for $a_{\alpha H}$, $a_{\beta H}$, a_{av}, and Δa (Table 2).

The results are compared with values reported for these radicals.[4,6] It is apparent that procedure (ii) gives by far the most satisfactory agreement with experiment. Indeed, since Matheson and Smaller [4] claim to have obtained approximate values for the individual lines from α- and β-hydrogen atoms in $\dot{C}H_2Me$, and record a value of 6 for Δa, one can postulate that for values of Δa much greater than 6, some resolution would be apparent. Certainly, values greater than 10 should give resolved spectra, and can accordingly be rejected. For the present, therefore, only results obtained by procedure (ii) will be reported for further estimations. Anticipating, one can say that procedure (ii) gives far closer agreement with experiment than the alternatives in all cases tested so far, procedure (i) being superior to procedure (iii).

The dearth of experimental results renders the task of interpreting spectra for more complex radicals difficult. For radicals derived from normal alkanes, such as $CH_3{\cdot}\dot{C}H{\cdot}CH_2R$ and $R{\cdot}CH_2{\cdot}\dot{C}H{\cdot}CH_2R'$, on a first approximation one can expect all β-hydrogen atoms to be equivalent. The delocalising effect of the β-alkyl groups is hard to estimate, but two extremes can be considered: (*a*) that the effect is zero, and (*b*) that the effect is equal to that of β-hydrogen.

Assumption (*a*) gives, by procedure (ii):

$$100 = \rho_C + 0{\cdot}062\rho_C + 5 \times 0{\cdot}078\rho_C$$

for $CH_3{\cdot}\dot{C}H{\cdot}CH_2R$, whence $\rho_C = 68{\cdot}9$ and therefore $a_{av} = 26{\cdot}3$ and $\Delta a = 5{\cdot}7$. Hence a poorly resolved 7-line spectrum having $a \approx 26{\cdot}3$ should be observed. Alger *et al.*[7] report a 7-line spectrum, $a = 27$, for radicals formed by high-energy radiation on the lower normal alkanes.

Similarly, for $R{\cdot}CH_2{\cdot}\dot{C}H{\cdot}CH_2R'$, $a_{av} = 27{\cdot}4$ and $\Delta a = 6{\cdot}0$. Hence a poorly resolved 6-line spectrum would be expected. In fact, the spectra obtained from higher alkanes after high-energy irradiation are complicated by the superposition of a set of relatively narrow lines on the central portion of the spectrum, and little can be said regarding the hyperfine splitting constants.[7]

Alternative (*b*) would mean that the parameters used for $\dot{C}HMe_2$ should be used. Hence $\rho_C = 65{\cdot}4\%$, $a_{\alpha H} = 20{\cdot}3$, and $a_{\beta H} = 25{\cdot}7$. Since, however, there are now only five β-hydrogen atoms, $a_{av} = 24{\cdot}8$. The value estimated by procedure (*a*) is thus closer to experiment, but the difference is not very large, so that no firm conclusions regarding hyperconjugation by β-alkyl groups can be drawn (see below).

The only unsaturated hydrocarbon radical whose spectrum is known is allyl, $CH_2{\cdot}CH{\cdot}CH_2{\cdot}$. Matheson and Smaller [4] report a value of 15·5 for the hyperfine splitting constant derived from the quintet ascribed to this radical. If the assumption were made that the unpaired electron was equally divided between the terminal carbons and had zero density elsewhere, calculations with procedure (ii) lead to $a_H = 13{\cdot}8$ for the quintet predicted. The experimental value is appreciably higher, and the discrepancy can be understood in terms of the postulate that there is a small negative spin-density on the central carbon atom. Use of $a = 15{\cdot}5$ gives $\rho_C = 50$, and hence the net spin-density on the methylene groups is 112·4%. This leads to a value of −12·4% on the central carbon atom, which can be compared with a recent theoretical estimate of −10·6%.[5] On this

[5] McConnell and Chesnut, *J. Chem. Phys.*,1 958, **28**, 107.
[6] Gordy and McCormick, *J. Amer. Chem. Soc.*, 1956, **78**, 3243.
[7] Alger, Anderson, and Webb, in the press.

basis, the central hydrogen atom should give rise to a splitting of about 3·8 gauss; this would appear as added broadening in the spectrum.

Turning to radicals of type $R_2\dot{C}Y$, we can, by using the above values [Table 1 (ii)], estimate the "delocalising power" of groups Y. The most extensive series of experimental results are for the aliphatic alcohols (Y = OH), the results being summarised in Part II.

Radicals derived from Alcohols.—From the value $a = 19$ for $\cdot CH_2\cdot OH$, $a_{\alpha H} = 19 = \rho_O \times 0{\cdot}31$, whence $\rho_O = 61{\cdot}3\%$. Hence from $100 = \rho_O = 2 \times 0{\cdot}062 \times \rho_O + A_{OH} \times \rho_O$, one gets $A_{OH} = 0{\cdot}50$. By using this value, together with the values for $a_{\alpha H}$ and $a_{\beta H}$ recorded in Table 2, the results shown in Table 3 (Nos. 1, 2, and 4) have been calculated. Agreement with experiment is well within experimental error and Δa for the radical from ethanol (No. 2) is so small that one would expect a fairly symmetrical 5-line spectrum.

In view of the uncertainty in the identification of the radicals [1] derived from propan-1-ol and higher alcohols the results cannot be used to test further the suitability of the procedure outlined above. However, the agreement found is such that one can postulate that any marked deviation from a_{av} estimated for a certain radical can be taken as a strong indication that the postulated radical is not, in fact, the correct one.

The experimental result for $\cdot CH_2\cdot CMe_2\cdot OH$ ($a = 24$) derived from *tert.*-butyl alcohol, though only approximate, can be used to obtain a rough value for the group $-CMe_2\cdot OH$. It turns out that $A \approx 0{\cdot}16$, and the agreement with experiment found when this value is used to estimate a_{av} for $MeCH\cdot CMe_2\cdot OH$ (Table 3, No. 13) indicates that this value is satisfactory. If one assumes that this delocalising power is equally shared between the β-methyl groups and β-hydroxyl, then $A_{\beta Me} \approx A_{\beta OH} \approx 0{\cdot}053$. This result for β-methyl is less than that for β-hydrogen (0·078) and is probably of the right order of magnitude.

By using these figures, the results in Table 3 (Nos. 3, 5, 7, 8, 9, 11, 12) have been derived. For radicals formed by loss of α-hydrogen the largest estimated value is 21 gauss, whilst when β- or γ-hydrogen is lost the minimum value is 24, and the usual value between 26 and 27 gauss. In Part I we attempted to identify radicals by a consideration of the number of lines in the electron-spin resonance spectrum. In several instances, notably for propan-1-ol, this criterion proved unsatisfactory. If, however, the magnitude of a can be used as an added criterion, selection of alternative radicals is often easier. For example, our value of 22 gauss for propan-1-ol is only compatible with structure No. 6 (Table 3); both Nos. 7 and 8 require values for a far larger than the experimental value. Fujimoto and Ingram [8] found 6 lines for radicals from propan-1-ol, with $a_{av} \approx 20$. Again, this value is too small for radicals formed by attack on β- or γ-hydrogen.

[The average value of 20 gauss is measured directly from the derivative curve presented.[8] However, a reconstruction of the experimental curve is also given, consisting of a set of 4 lines, each split into a triplet. From the derivative curve, we estimate a(4-lines) ≈ 23 and a(3-lines) ≈ 15. However, the authors attribute this spectrum to the radical $CH_3\cdot\dot{C}H\cdot CH_2\cdot OH$, and quote $a_{CH_3} = 29$ and $a_{CH_2} = 20$. They conclude that the α-hydrogen atom gives no detectable interaction. From these quoted values, $a_{av} = 25{\cdot}4$, which is certainly possible for the radical depicted. We cannot discover which set of data is correct since we invariably obtain a 5-line spectrum from propan-1-ol radicals.]

The 6-line spectrum from butan-2-ol was assigned to either radical No. 10 or No. 11.[1] The experimental value of 21 for a, however, fits well with No. 10 and eliminates No. 11.

In Part II we recorded examples of complex spectra sometimes detected for ethanol and propan-2-ol radicals. It was pointed out that one way of building up these spectra was to superimpose spectra of 5 lines ($a \approx 25$) and 4 lines ($a \approx 27$) respectively upon the normal spectra. These results are in close agreement with those expected for radicals formed by attack on β-hydrogen (Nos. 3 and 5 respectively).

Another result from the field of alcohol radicals which can now be treated quantitatively

[8] Fujimoto and Ingram, *Trans. Faraday Soc.*, 1958, **54**, 1304.

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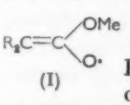
is the 4-line spectrum from radicals formed by attack of hydroxyl radicals on allyl alcohol. We have already noted that the relatively small value for a (about 13 gauss) is best understood if the radical $CH_2{:}\dot{C}H{\cdot}CH{\cdot}OH$ is formed by attack on allylic hydrogen.[2] Since a symmetrical 4-line spectrum is obtained, $a_{\alpha H} \approx a_{\gamma H}$ and therefore $\rho_{\alpha C} = \rho_{\gamma O} = \rho_C$. Proceeding as for the allyl radical and using $a_{av} = 13$, we get $13 = 0{\cdot}31\rho_C$, whence $\rho_O = 42$. The total electron density on the outer carbon atoms and attached atoms is then equal to $42 \times 2{\cdot}686 = 112{\cdot}7$, and therefore the electron density on the central C–H group is 12·7%. This value being used, the hyperfine splitting constant for the central hydrogen is found to be 3·7 gauss. The doublet splitting caused by this interaction would be too small to show in our spectra.

Other Radicals.—Table 4 gives some values for A_Y, Y being attached directly to the carbon atom carrying the unpaired electron. The value for $-O^-$ is taken from $a = 16$ for the triplet obtained from $\cdot CH_2{\cdot}O^-$.[7] That $-O^-$ is more effective than –OH is not surprising, since the extreme structures $:\bar{C}H_2{-}O\cdot$ and $:\bar{C}H_2{-}\dot{O}H^+$ only involve charge separation in the latter case.

The values for CO_2Me and CN are derived from results reported for the radicals $HO{\cdot}CH_2{\cdot}\dot{C}Me{\cdot}CO_2Me$ and $HO{\cdot}CH_2{\cdot}\dot{C}Me{\cdot}CN$ respectively.[9] The result for $-CO_2Me$ is only slightly greater than that for –OH, which is unexpected, since this group is able to effect delocalisation by means of structures such as (I). The value for A_{CN} can be used to predict a value for a_{av}, for radicals from polyacrylonitrile, $R{\cdot}CH_2{\cdot}\dot{C}H{\cdot}CN$. This gives $a_{av} = 18{\cdot}1$ and $\Delta a = 4{\cdot}2$. Although we have only obtained a single broad line from radicals from polyacrylonitrile, Abraham, Ovenall, and Whiffen [10] report a 7-line spectrum with $a = 18{\cdot}5$. It is not easy to understand why 7 lines should be observed, but the value for a is very close to the predicted value.



(I)

The figure for $-CO{\cdot}NH_2$ is very tentative. It was obtained from data quoted by Luck and Gordy [11] for the triplet and quintet which were observed after acetamide and propionamide had been exposed to X-radiation. If one postulates that the radicals responsible for these spectra are $\cdot CH_2{\cdot}CO{\cdot}NH_2$ and $CH_3{\cdot}\dot{C}H{\cdot}CO{\cdot}NH_2$ respectively, then this value results in both instances.

A variety of results is available relating to radicals formed by high-energy irradiation of amino-acids. Waring [12] has made a careful study of α-amino*iso*butyric acid and presents convincing evidence that the main radical produced is $Me_2\dot{C}{\cdot}CO_2^-$ (or $Me_2\dot{C}{\cdot}CO_2H$). Single-crystal studies show that the hyperfine splitting constant is not quite isotropic and give an average value of 23·5 gauss. Using this value, we get $A_{CO_2^-}$ (or A_{CO_2H}) $\approx 0{\cdot}2$. If we assume that the same type of break-up occurs with other amino-acids, the 5-line spectrum from alanine ($a_{av} \approx 25$) and the triplet from glycine ($a \approx 20$) can be assigned to the radicals $CH_3{\cdot}\dot{C}H{\cdot}CO_2^-$ and $\cdot CH_2{\cdot}CO_2^-$ respectively. Using $A_{CO_2^-} = 0{\cdot}2$, we get $a_{av} = 25$ for the former and $a = 23{\cdot}4$ for the latter. Whilst the former result is compatible with experiment, the latter is far too large. It seems possible that in this case a different radical is involved.

Discussion.—The interaction which occurs between an unpaired electron in a p-orbital on trigonally hybridised carbon and protons bonded to this carbon has been discussed fully. The results obtained from aromatic radicals and radical ions in dilute fluid solution, under conditions such that all dipolar interactions would average to zero, show conclusively that contact interaction (whereby an unpaired electron is left in a 1s-state on hydrogen) is of considerable importance.

McConnell [5] has been able, by use of the equation $a_N = Q\rho_\pi$ (where a_n is the hyperfine

[9] Ingram, Symons, and Townsend, *Trans. Faraday Soc.*, 1958, **54**, 409.
[10] Abraham, Ovenall, and Whiffen, *Arch. Sci.*, 1957, **10**, 84.
[11] Luck and Gordy, *J. Amer. Chem. Soc.*, 1956, **78**, 3240.
[12] Waring, personal communication.

splitting constant and ρ_n the unpaired electron density on $C_{(n)}$), to correlate many results and to obtain important information regarding ρ_n. Various theoretical and experimental values for Q have been proposed.[5,13] McConnell favours the numerical value of 22·5 obtained from the benzene negative ion.[5] We have found that an average value of 31 gauss gives a satisfactory fit for data from a number of aromatic positive and negative ions.[14]

If, as in (i) above, one assumes that $\rho_n = 1$ for $\cdot CH_3$ then $Q = 26$, a result which is remarkably close to the value derived from aromatic radicals and radical-ions. However, somewhat better agreement between experimental and estimated values is obtained if one allows for the fact that α-hydrogen atoms can delocalise the unpaired electron. That means that in the radical $\cdot CH_3$, ρ_n is not taken as unity but as some smaller value, depending upon the delocalising power of α-hydrogen atoms [see process (ii) above]. On this basis, an estimate of the hyperfine splitting constant for the planar radical $R_2\dot{C}H$ gives $a_{\alpha H} \approx 30$ gauss if it is assumed that the R groups do not interact. One conclusion that can be drawn is that $a_{\alpha H} \leqslant 30$ gauss in any radical having an unpaired electron in a p-orbit on trigonally hybridised carbon.

This conclusion is not true if the radical is pyramidal, but theoretical calculations by Karplus [15] have shown that a small divergence from planarity would make very little difference, and that even in the extreme case in which tetrahedral configuration is retained, only a small increase in a would result.

Another conclusion is that α-hydrogen atoms are bound to interact strongly with the unpaired electron. For saturated radicals of the type discussed above, this interaction would probably give a value for $a_{\alpha H}$ greater than 15 gauss, and hence the assumption that in radicals of structure $CH_3\cdot\dot{C}H\cdot[CH_2]_n\cdot OH$ the α-hydrogen atom will not contribute to the observed spectrum seems to be unjustified.[8] However, in some circumstances β-hydrogen atoms may not interact appreciably: this is discussed in Section II.

The results reported by Matheson and Smaller [4] for $\cdot CH_3$ and $\cdot CMe_3$, used in the above manner, make it clear that $a_{\alpha H}$ and $a_{\beta H}$ will generally be so nearly equal that, because of the breadth of the individual lines, the measured spectrum will be an unresolved superposition of the lines from α- and β-hydrogen atoms and will closely resemble the spectrum to be expected from a radical in which α- and β-hydrogen atoms are equivalent. Several workers have been loth to accept this coincidence of near equality and have, instead, postulated the existence of radicals in which the hydrogen atoms are all completely equivalent. For example, Gordy *et al.*[6] have suggested that, because of the symmetry of the sextet obtained from $\cdot CH_2Me$, a type of rapid intramolecular exchange of hydrogen or internal hydrogen bridging occurs. Matheson and Smaller's results [4] show that this postulate is not required, and indeed there is strong experimental evidence against it. Thus McNesby, Drew and Gordon [16] have shown that, even at high temperatures (365—506°), hydrogen atoms cannot be transferred intramolecularly in the *n*-butyl radical. A rapid equilibration at 72° K is therefore out of the question.

Another example is the ion $C_2H_4^+$, which Gordy and his co-workers have frequently postulated in order to explain a 5-line spectrum ($a \approx 20$) which is observed during high-energy irradiation of certain organic compounds. For instance, Luck and Gordy [11] suggest that this radical-ion is formed during *X*-irradiation of solid ethanol. Their spectrum is almost identical with ours,[1] and we have presented strong evidence in favour of the radical $CH_3\cdot\dot{C}H\cdot OH$. It is difficult to see how $C_2H_4^+$ could be formed under the very mild conditions used in our experiments. Another argument against $C_2H_4^+$ is that the experimental value of about 21 for a is too large. This value for a corresponds to $X_{\alpha H} = 0{\cdot}42$. Since all the results so far obtained for neutral, positive, and negative radicals give values between 0·22 and 0·31 for $X_{\alpha H}$, this value is excessively large and hence

[13] Weissman, *J. Chem. Phys.*, 1954, **22**, 1378.
[14] Carrington and Symons, *J.*, in the press.
[15] Karplus, to be published.
[16] McNesby, Drew, and Gordon, *J. Chem. Phys.*, 1956, **24**, 1260.

one can conclude that the spectrum is not that of $C_2H_4^+$. Bersohn [17] has calculated a value of 8·4 gauss for a. Using the value $X_{\alpha H} = 0{\cdot}31$ calculated above, we would predict $\rho_O = 44{\cdot}4\%$ on each carbon atom, and hence that $a \approx 13{\cdot}7$ for $C_2H_4^+$.

It has been assumed that in saturated radicals, only α- and β-hydrogen atoms interact with the unpaired electron. If β-methyl groups can release electrons significantly then there will be some contribution from γ-hydrogen atoms. However, on using the value $A_{\beta Me} \approx 0{\cdot}053$ estimated above it is apparent that γ-hydrogen interaction will be an order of magnitude smaller than that from α- and β-hydrogen atoms. If, for steric reasons, hydrogen from another molecule or another portion of the same molecule is forced close in to the orbit of the unpaired electron, it might interact specifically and hence give rise to detectable splitting. However, no evidence of this process has yet been presented.

II. It is usually assumed that β-hydrogen atoms attached to a particular carbon atom give equal splitting; *i.e.*, they interact equally with the unpaired electron. This is only possible if rotation about the carbon–carbon bond is rapid. If, for some reason, rotation is restricted, such β-hydrogen atoms might no longer be equivalent, and I attempted to explain the curious 9-line spectrum obtained from poly(methyl methacrylate) in terms of this principle.[9]

This principle is assumed in many instances. For example, β-hydrogen interaction is not observed and never postulated for unsubstituted aromatic radical-ions. This is because all the hydrogen atoms lie in the nodal plane of the π-orbital containing the unpaired electron, and hence overlap between this and the C–H bonding orbital is negligible. A similar example is the central hydrogen atom of the radical from allyl alcohol considered earlier. This is in the nodal plane of the π-orbital containing the unpaired electron and therefore cannot interact by a hyperconjugation process.

There are other less clear-cut examples. The hydroxyl hydrogen in alcohol radicals of type $R_2\dot{C}{\cdot}OH$ is effectively a β-hydrogen and would surely interact in the usual way in the general case. However, there is considerable evidence that interaction is very weak. Thus the radical derived from methoxide gives a spectrum which is almost identical with that from radicals from methanol, and ethanol deuterated on the hydroxyl group gives a spectrum identical with non-deuterated ethanol.[7] Our calculations suggest that the hydroxyl group has a large delocalising power. This probably arises through overlap between a fully occupied p–π oxygen orbital and the half-filled p-orbital on carbon. In order for this overlap to be large, the O–H bond must be constrained to lie in the nodal plane of the molecular orbital thus formed, and hence will not interact strongly.

A similar argument goes some way to explaining why the electron-spin resonance spectrum of $HO_2{\cdot}$ is not a doublet.[1] If one accepts that the extreme structure $\cdot O{-}O{-}H$ is an important contributor to the actual structure, then the main interaction between the unpaired electron and the proton should be by hyperconjugation. However, once again, in order to obtain efficient overlap with the filled p–π oxygen orbital, the hydrogen must lie in the nodal plane of the unpaired electron, thus removing the possibility of hyperconjugation.

The value $A_{OH} = 0{\cdot}5$ being taken as a measure of the unpaired-electron density on the OH group, an approximate value for splitting to be expected from hydroxyl-hydrogen due to configurational interaction can be obtained. For example, the radical from propan-2-ol has $\rho_O = 50{\cdot}8$ and hence $\rho_{OH} = 25{\cdot}4$. If $a_{OH} \approx a_{\alpha H} = 0{\cdot}31$, then $a_{OH} \approx 7{\cdot}9$ gauss. A splitting of this magnitude would be on the verge of detection, and is probably an overestimate. (By the same argument, the doublet splitting for ·OH should be about 30 gauss. Matheson and Smaller [18] observed a doublet having $a = 10$ gauss after exposing ice and hydrogen peroxide to γ-rays. This is only detectable at 4° K and may well be due to hydroxyl radicals. If this is the case then our estimate of 7·9 for a_{OH} in $Me_2\dot{C}{\cdot}OH$ is too large.)

[17] Bersohn, *J. Chem. Phys.*, 1956, **24**, 1066.
[18] Matheson and Smaller, *ibid.*, 1955, **23**, 521.

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No calculations concerning the way in which a for a given β-hydrogen atom will vary with θ have yet been published. Earlier, we assumed that if a C–H bond was fixed in a direction perpendicular to the nodal plane of the unpaired electron then it would give a splitting equal to that of a free β-hydrogen atom.[9] It was also assumed that the interaction from a C–H bond at 30° to the plane would be negligible. These assumptions were arbitrary, and may be incorrect. On a semi-intuitive basis one might guess that the interaction would follow a $\cos^2\theta$ law. If that were so, then, the interaction for a hydrogen lying at 90° to the nodal plane ($\theta = 0$) being taken as 1, the relative values for $\theta = 30°$, 60°, and 90° will be 0·75, 0·25, and zero. In order to relate these relative values to experiment a value for a " free " hydrogen atom is required. It can be shown that if the three hydrogen atoms in a methyl group make angles θ_1, θ_2, and θ_3 to the normal, then $\cos^2\theta_1 + \cos^2\theta_2 + \cos^2\theta_3 = 1{\cdot}5$. Thus the net interaction for three equally interacting β-hydrogen atoms is 1·5, which gives a value of 0·5 for each.

If this argument is true, then the interpretation of the 9-line spectrum for poly(methyl methacrylate) [9] requires revision. The spectrum, assigned to the radical $R{\cdot}CH_2{\cdot}\dot{C}Me{\cdot}CO_2Me$, consists of 5 lines ($a = 21$) together with 4 lines ($a = 21$) which are somewhat weaker. The splitting between adjacent lines is thus 10·5. In order to interpret this spectrum, two structures were proposed, one having the group R at 90° to the plane (which contains the methyl and methylene carbon atoms together with the methoxycarbonyl group) and the other having one of the C–H bonds at 90° to the plane. In each case the methyl group is considered to be freely rotating, and hence $a_{Me} = 21$. However, if the $\cos^2\theta$ dependence is even approximately correct, these structures would not combine to give the required spectrum. The former has two equivalent hydrogen atoms at 30° to the plane ($\theta = 60°$). Relative to the average value of 21, the hyperfine splitting constant will be $21 \times 0{\cdot}25/0{\cdot}5 = 10{\cdot}5$. Therefore each of the four lines from the methyl group will be split into three, giving a final spectrum of nine lines, $a = 10{\cdot}5$ with relative intensities 1, 2, 4, 6, 6, 6, 4, 2, 1. The number of lines and the splitting are correct, but the relative intensities are wrong, since in the experimental curve the ratios are approximately 3, 2, 12, 6, 18, 6, 12, 2, 3.

The latter structure can be rejected since one of the two methylene-hydrogen atoms (H_1) will have $a_1 = 21 \times 1/0{\cdot}5 = 42$, and the other ($H_2$) will have $a_2 = 21 \times 0{\cdot}25/0{\cdot}5 = 10{\cdot}5$. This will give a spectrum of 12 lines having $a = 10{\cdot}5$.

A model of this radical reveals, not only that rotation about the C–C bond will be extremely difficult, but also that the least hindered conformation will be one in which the bulky R group is at 90° to the plane. This structure alone is not satisfactory, as shown above. However, if one allows a twist of 15° to either side of this symmetrical arrangement, then two other mutually equivalent structures will also contribute, in which H_1 is at 15° and H_2 at 45° to the plane (or *vice versa*); H_1 will now give a negligible splitting, since $a_1 = 21\cos^2 75°/0{\cdot}5 = 2{\cdot}8$. H_2 will have $a_2 = 21\cos^2 45°/0{\cdot}5 = 21$. These structures will therefore give rise to a simple 5-line spectrum having $a = 21$. If each position is of equal importance, the final spectrum will consist of 9 lines having relative intensities 3, 2, 12, 6, 18, 6, 12, 2, 3. This result is very close indeed to the experimental spectrum.

It is tempting to apply this concept of hindered rotation to some of the simple radicals studied in Part II. In general, the probability that a β-hydrogen atom will not give an averaged interaction will decrease in the order tertiary > secondary > primary, for two reasons. First, the other groups are certain to be more bulky than hydrogen, and secondly, the amount of twist required to obtain equivalence decreases in this order. A single C–H bond must be twisted through 90° to pass from maximum to minimum interaction. In contrast, a methyl group needs to be rotated through only 30°.

We conclude that a methyl group is least likely to display differences due to hindered rotation. An attempt has been made to explain the 6-line spectrum sometimes observed for radicals from propan-2-ol [1] in terms of this principle of hindered rotation. The value $a = 22$ is assigned to six hydrogen atoms and $a = 9$ to the seventh.[8] If our reasoning is

even approximately correct, even if the rotation of a methyl group was hindered in this way, it is extremely hard to understand why one hydrogen atom should have its interaction reduced so drastically whilst the other two still give an averaged interaction. It is suggested [8] that this process is important at 77° K but insignificant at 110° K, at which temperature the normal 7-line spectrum for propan-2-ol is obtained. However, we have observed the 7-line spectrum at 77° K.

One radical in which restricted rotation should play an important part is that derived from *cyclo*hexanol. It is certainly possible to build up the observed 6-line spectrum [2] by use of the above principle on the basis that the radical is formed by loss of an α-hydrogen atom. However, the observed spectrum is so poorly resolved that relative line intensities cannot be measured and therefore detailed discussion is not warranted. The alternative, that attack is on γ- or δ-hydrogen, would certainly explain the presence of 6 lines, but the observed splitting of 20 gauss is at least 5 gauss too small for this postulate.

III. *Secondary Radical Reactions in Solids.*—Intense electron-spin resonance spectra are often obtained from organic solids after exposure to high-energy radiation, and these spectra are often remarkably simple. This simplicity is at first sight surprising because, in general, two different paramagnetic species are to be expected, and their superimposed spectra would normally give a complex pattern.

It is often suggested, by analogy with the better understood behaviour of ionic crystals, that electrons, detached during the primary process, are trapped elsewhere in the solid. Two difficulties arise: first, the trapped electrons should give rise to an electron-spin resonance signal, and secondly, a radical positive ion rather than a neutral radical is the second product. It is possible that the electron-spin resonance spectrum from the trapped electrons is broad and escapes detection, but it is by no means clear why this should be. We have obtained spectra with line-widths (between points of maximum slope) of the order of 4 gauss from glasses formed by freezing blue solutions of alkali metals in ammonia,[19] and it is hard to understand what features in simple organic solids would be able to increase this width so drastically.

The remarkable similarity between spectra obtained from neutral radicals formed by abstraction of hydrogen by hydroxyl radicals and radicals formed from the same organic compounds by high-energy radiation leaves little doubt that they are derived from identical radicals. The spectra obtained from methanol, ethanol, propan-1-ol, and propan-2-ol, for example, are all very similar whatever method is used.[2,7] Since hydroxyl radicals are able to abstract hydrogen from alcohols at 77°,[2,20] it is reasonable to postulate that other highly reactive radicals will also be able to do so. On this basis, one can formulate the reaction for alcohols as follows:

$$R_2CH{\cdot}OH + h\nu \longrightarrow R_2\dot{C}{\cdot}OH + H{\cdot}$$
$$H{\cdot} + R_2CH{\cdot}OH \longrightarrow H_2 + R_2\dot{C}{\cdot}OH$$

Reactions such as these may occur before the radicals have lost their excess of energy possessed at the time of formation, in which case the final products will be close neighbours. If this is so, an explanation can be found for a remarkable difference in the optical properties of alcohol glasses containing trapped alcohol radicals. As noted earlier,[20] when solutions of hydrogen peroxide in primary and secondary alcohols are irradiated a violet colour is observed due to an absorption band of low intensity with a maximum absorption at about 5000 Å. Alger *et al.*[7] find very similar visible spectra to ours, but there is one marked difference. Colours formed during high-energy irradiation are rapidly bleached by visible light, but similar colours obtained by peroxide photolysis are unaffected by visible light. Both procedures give paramagnetic glasses displaying nearly identical electron-spin resonance spectra. The photobleached glasses still give the same spectra, not markedly

[19] Clark and Symons, to be published.
[20] Symons and Townsend, Part I, *J.*, 1959, 263.

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diminished in intensity, and, because of this, Alger *et al.*[7] justifiably conclude that the radical which gives rise to the electron-spin resonance spectrum is *not* the species responsible for the violet colour. However, for a variety of reasons, we have concluded the reverse, namely, that free radicals having the general structure $R_2\dot{C}\cdot OH$ are responsible for both the electron-spin resonance and the visible spectra.[20]

We have already postulated [20] that if radicals are formed in pairs, those in each pair may sometimes be so close together that the net magnetic field experienced by either radical is equal to the applied field plus a small increment from the neighbouring radical. This extra field will be a function of the distance between the paired radicals and the orientation of the pairs relative to the direction of the applied field. Since both these parameters are certain to vary over a wide range this interaction could broaden the resonance signal beyond the limits of detection.

Such magnetic interaction would not appreciably alter the visible and ultraviolet spectra of the radicals concerned. A situation could therefore arise in which a large number of radicals, giving rise to an intense violet colour, are paired off in such a way that no electron-spin resonance spectrum can be detected. At the same time a relatively small number of radicals are envisaged as being trapped singly so that no modification of the applied field occurs. The effect of these radicals will therefore be cumulative and a detectable electron-spin resonance spectrum should result. Finally, since most of these radicals are paired closely together, excitation by visible light could so dispose the radicals that recombination or disproportionation takes place: this would result in a great decrease in visible absorption but the electron-spin resonance absorption would be unaffected or become better resolved. The small specimens used by Alger *et al.*[7] are sometimes so deeply coloured that they appear black, and yet the intensity of the electron-spin resonance spectrum is such that on a comparable scale, our specimens would probably seem colourless. Accordingly, it is postulated that radicals produced by hydroxyl-radical attack are not sufficiently close to interact magnetically. This theory is speculative but does seem to account for results which otherwise appear to be mutually contradictory.

Two other examples in which light excitation may lead to further reaction will be considered. The first is also drawn from the work of Alger *et al.*[7] When an irradiated methanol glass is exposed to intense ultraviolet light the triplet attributed to $\cdot CH_2\cdot OH$ is lost, and a doublet with a splitting of 136 gauss appears instead. No explanation of this phenomenon has been offered. It seems likely that the original radicals are undergoing photolysis, and two modes of decomposition seem reasonable:

$$\cdot CH_2\cdot OH + h\nu \longrightarrow CH_2O + H\cdot \quad \ldots\ldots\ldots\ldots \quad (1)$$

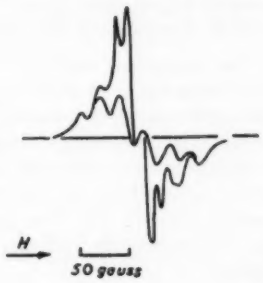
or

$$\cdot CH_2\cdot OH \longrightarrow \cdot CH + H_2O \quad (2)$$

We would not expect that hydrogen atoms would be trapped under these conditions, but rather, that they would attack methanol to re-form the radical $\cdot CH_2\cdot OH$. Accordingly, it is suggested that the radical $\cdot CH$ is the species giving rise to the doublet. The splitting of 136 gauss is surprisingly large, but is not out of the question since the structure of this intermediate is very different from the radicals so far considered. The doublet is remarkable also because it is asymmetric, one band being much broader than the other. Recently McGarvey [21] has applied a theory proposed by McConnell [22] to explain a similar phenomenon found for solutions of copper chelates. This theory is based upon the supposition that the complex is tumbling, the asymmetry in line widths being a function of the rate of tumbling and the anisotropy of the resonance. The $\cdot CH$ radical might well be small enough to be moving in this way even in a solid at low temperature, in which case the asymmetry in hyperfine lines could be explained by the same theory.

[21] McGarvey, *J. Phys. Chem.*, 1957, **61**, 1232.
[22] McConnell, *J. Chem. Phys.*, 1956, **25**, 709.

The other example of a light-induced secondary reaction is drawn from the effect of prolonged irradiation (3650 Å) upon the electron-spin resonance spectrum of radicals from allyl alcohol, $CH_2{:}CH{\cdot}\dot{C}H{\cdot}OH$. The normal spectrum is a quartet having $a \approx 13$ gauss. However, on prolonged irradiation further lines appear on the edges with a splitting of about 24 gauss. A typical spectrum is shown in the Figure, together with a postulated 6-line spectrum, having $a \approx 24$ (broken line). The radical $CH_2{:}CH{\cdot}\dot{C}H{\cdot}OH$ is yellow [20]



First derivative of the electron-spin resonance spectrum from photolysed solid solutions of hydrogen peroxide in allyl alcohol, after prolonged irradiation.

and hence will certainly absorb in the 3650 Å region. It is postulated that light excitation renders the radical sufficiently reactive to be able to add to a neighbouring alcohol molecule:

$$CH_2{:}CH{\cdot}\dot{C}H{\cdot}OH + CH_2{:}CH{\cdot}CH_2{\cdot}OH \longrightarrow CH_2{:}CH{\cdot}CH(OH){\cdot}CH_2{\cdot}\dot{C}H{\cdot}CH_2{\cdot}OH$$

(the alternative of attack on allylic hydrogen would lead to no net change). We would predict a spectrum of 6 lines for this radical, and estimate $a_{av} \approx 25{\cdot}5$.

Fujimoto and Ingram [8] have also observed this phenomenon, but suggest that the new lines which appear on the edges of the original spectrum are part of a superimposed 5-line spectrum. According to our measurements, this spectrum would have $a_{av} \approx 30$ gauss, which is very large. They suggest [8] that the species responsible is a diradical formulated as

$$HO{\cdot}CH{:}CH{\cdot}\dot{C}H_2 \cdots \dot{C}H_2{\cdot}CH{:}CH{\cdot}OH$$

We cannot understand why a light-induced approach of radicals should stop, when a minute continuation would give a stable molecule. However, although the proposed structure is somewhat obscure, the unpaired electrons still appear to be in molecular orbitals covering the whole of each molecule, in which case a 7-line spectrum having $a \approx 13$ should result (provided that the diradical nature of the species was such that it would in fact give rise to an isotropic spectrum having a g-value of 2·00, and no zero-field splitting).

Conclusion.—Many of the concepts considered are undoubtedly extreme oversimplifications of the truth. Nevertheless it is hoped that, at least in some instances, they may lead towards a better understanding of a complex subject.

This work was carried out during the tenure of a visiting associate professorship at the University of British Columbia. We acknowledge the kind hospitality of Professor C. A. McDowell and his colleagues, and thank Drs. J. Coupe and R. Hockstraesser for valuable help.

THE UNIVERSITY, SOUTHAMPTON. [*Received, June 30th*, 1958.]

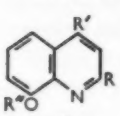
49. *Steric Hindrance in Analytical Chemistry. Part V.* A New 2-Substituted 8-Hydroxyquinoline (Oxine).*

By H. Irving and D. J. Clifton.

2-(1-Ethylpropyl)-8-hydroxyquinoline has been prepared from 2-(1-ethylpropyl)-8-methoxyquinoline, and the sensitivity of its precipitation reactions towards copper, zinc, aluminium, and indium compared with those of oxine (8-hydroxyquinoline), 2-methyloxine, and 2-phenyloxine.

Although the analytical reactions of 2-methyloxine (I; R = Me, R′ = R″ = H) are distinguished from those of oxine itself by its failure to give an insoluble tris-complex with aluminium, its reactions towards other ions are in no way exceptional.[1] A 2-methyl substituent decreases the stability of all metal complexes of 8-hydroxyquinolines so far studied,[2] owing to steric hindrance to co-ordination around the central ion. It was clearly of interest to see whether the small increase in selectivity effected by a 2-methyl group—and exhibited only in connection with the very small Al^{3+} ion—would be extended to ions of larger ionic radius by increasing the spatial requirements of the substituent adjoining the chelating group.

2-(1-Ethylpropyl)-8-hydroxyquinoline (I; R = $CHEt_2$, R′ = R″ = H) was obtained as a low-melting solid by the decarboxylation of 2-(1-ethylpropyl)-8-hydroxyquinoline-4-carboxylic acid[3] (I; R = $CHEt_2$, R′ = CO_2H, R″ = H). Better overall yields were obtained by the successive demethylation and decarboxylation of 2-(1-ethylpropyl)-8-methoxyquinoline-4-carboxylic acid (I; R = $CHEt_2$, R′ = CO_2H, R″ = Me) which was prepared in 30% yield by the condensation of *o*-anisidine with pyruvic acid and α-ethylbutyraldehyde.



(I)

No precipitate was formed when an acidic solution of the new reagent and aluminium nitrate was gradually basified, provided tartrate was present to hold up hydroxide or other basic salts. By potentiometric titration of a solution in 0·1N-nitric acid in the presence, and in the absence, of aluminium ions it was established that the formation of any metal complex was too slight to be detectable. As in the analogous titration of a mixture of aluminium and 2-methyloxine, the white precipitate formed at pH ~4·2 was essentially of aluminium hydroxide.

The sensitivity of the reactions of 2-(1-ethylpropyl)-8-hydroxyquinoline towards a few typical cations was determined in three buffer solutions A, B, and C of pH 5·14, 8·4, and 12·4 respectively. The procedures previously described were adopted[1,4] apart from an increase in the amount of alcohol present which was found necessary to compensate for the lower solubility of the reagent in water: on this account the sensitivities quoted may be somewhat lower than if they had been determined under the conditions to which the bulk of the data in the Table refers.

2-(1-Ethylpropyl)-8-hydroxyquinoline gives brown and yellowish-green complexes respectively with Cu^{2+} and Zn^{2+}, and the sensitivity of its reactions with these cations is similar to that of 2-methyl- and 2-phenyl-oxine. However, like all 2-substituted oxines so far studied, it fails to give an insoluble complex with Al^{3+}. With the appreciably larger ion, In^{3+}, a yellow complex is readily formed and the sensitivity of this reaction in buffer B is comparable with that for oxine and 5-methyloxine and distinctly greater than for 2-methyloxine. In buffer A the effect is equally marked and the new reagent is exceptional in giving a precipitate in the very alkaline buffer C. This could well be due to the effect

* Part IV, *J.*, 1958, 3540.

[1] Irving, Butler, and Ring, *J.*, 1949, 1489.
[2] Irving and Rossotti, *J.*, 1954, 2910; (Miss) Massey-Beresford, B.Sc. Thesis, Oxford 1955.
[3] Hollingshead, personal communication.
[4] Irving and Rossotti, *Analyst*, 1955, **80**, 245.

of the higher basicity conferred by the 2-alkyl substituent, reinforced by the " weighting effect " of the large alkyl group: together these two factors appear to dominate the

Sensitivities of reactions between metals and homologues of 8-hydroxyquinoline (oxine).

	Copper			Zinc		
Reagent	A	B	C	A	B	C
Oxine	1·1—0·4	1·1—0·4	1·1—0·4	1·1—0·4	1·1—0·4	10·6—4·2
2-Methyloxine	2·0—0·4	1·0—0·4	20·5—10·3	21·0—10·6	1·0—0·4	10·6—2·1
2-(1-Ethylpropyl)oxine	2·0—1·0	2·0—1·0	2·1—1·0	20·4—10·3	2·1—1·0	2·0—1·0
2-Phenyloxine	1·0—0·4	1·0—0·4	2·0—1·0	10·6—4·2	2·1—1·1	2·1—2·1
5-Methyloxine	1·0—0·4	1·0—0·4	1·0—0·4	10·6—4·2	—	N.P.

	Aluminium			Indium		
Reagent	A	B	C	A	B	C
Oxine	4·3—1·7	4·3—1·7	N.P.	5·26—3·6	5·2—3·6	N.P.
2-Methyloxine	N.P.	N.P.	N.P.	18·5—7·4	18·5—7·4	N.P.
2-(1-Ethylpropyl)oxine	N.P.	N.P.	N.P.	6·96—5·2	5·2—3·6	16·0—7·0
2-Phenyloxine	N.P.	N.P.	N.P.	—	—	—
5-Methyloxine	0·9—0·4	—	N.P.	1·85—0·95	5·3—3·6	N.P.

N.P. No precipitate was observed. Data for 2-methyl- and 2-phenyl-oxine from ref. 1. The figures are the smallest concentration of metal (in μg./ml.) which gave a perceptible precipitate under the standard condition [1,4] and the largest concentration which just failed to do so.

steric factors which are caused by substitution in the 2-position which operate to prevent chelation [1,2] and decrease the sensitivity of the reaction. The effect of steric factors in reducing sensitivity is clearly shown in the data for the two position-isomers, 2- and 5-methyloxine. That 2-(1-ethylpropyl)oxine reacts with the indium ion almost as readily as oxine itself and appreciably more readily than 2-methyloxine, despite the steric hindrance to co-ordination demonstrated by its failure to form a tris-complex with the smaller aluminium ion, must largely be due to a weighting effect. However it should not be overlooked that the sensitivity of such reactions depends both on the stability of the chelated complex and on its intrinsic solubility,[4] and a full interpretation requires an assessment of these effects separately.

It is to be expected that a 2-alkyl substituent in a substituted oxine would, on chelation, adopt that conformation which minimises steric hindrance to co-ordination. In the group $CHEt_2$ rotation of the ethyl groups can produce a 2-substituent with a much smaller interference volume than would appear at first sight. With a tertiary carbon atom in this position, steric effects should be more pronounced. Experiments with 2-(*tert.*-butyl)-8-hydroxyquinoline (I; R = Bu^t, R′ = R″ = H) to test this hypothesis will be reported later.

Experimental

2-(1-*Ethylpropyl*)-8-*methoxyquinoline*-4-*carboxylic Acid*.—A mixture of α-ethylbutyraldehyde (44 g.) and pyruvic acid (24 g.) in ethanol (100 ml.) was added to a solution of redistilled *o*-anisidine (45·2 g.) in ethanol (400 ml.), and the whole heated under reflux for 17 hr. When cold the solution was seeded. Yellow crystals (30·4 g.) slowly separated. On recrystallisation from boiling ethanol (charcoal), 2-(1-*ethylpropyl*)-8-*methoxyquinoline*-4-*carboxylic acid* separated as yellow needles, m. p. 230° (Found: C, 70·3; H, 7·1; N, 5·3. $C_{16}H_{19}O_3N$ requires C, 70·3; H, 7·0; N, 5·1%).

2-(1-*Ethylpropyl*)-8-*hydroxyquinoline*-4-*carboxylic Acid*.—The methoxy-compound (3·5 g.) was heated under reflux for 4 hr. with fuming hydrobromic acid (20 ml.). The resulting clear solution was cooled, exactly neutralised with 2N-sodium hydroxide, and kept overnight in a freezing mixture. A greenish-yellow solid separated (18 g.). After recrystallisation, once from ethanol and twice from glacial acetic acid, 2-(1-ethylpropyl)-8-hydroxyquinoline-4-carboxylic acid was obtained as yellow crystals, m. p. 204°, which did not depress the m. p. of a specimen prepared from *o*-aminophenol, pyruvic acid, and α-ethylbutyraldehyde [3] (Found: C, 68·8; H, 7·4. Calc. for $C_{15}H_{17}O_3N$: C, 68·7; H, 7·4%).

2-(1-*Ethylpropyl*-8-*hydroxyquinoline*.—(a) *By decarboxylation of* 2-(1-*ethylpropyl*)-8-*hydroxyquinoline*-4-*carboxylic acid*. The acid (5·6 g.) was distilled *in vacuo* over a free flame.

The dark brown oily distillate solidified to a yellow mass, m. p. 130° (2·3 g.), which was extracted with hot dilute hydrochloric acid. Upon neutralisation with sodium carbonate the acid extract deposited a brown solid (1 g.), m. p. 44°. Recrystallisation from methanol and steam distillation gave white 2-(1-*ethylpropyl*)-8-*hydroxyquinoline*, m. p. 49° (Found: C, 78·0; H, 8·0; N, 6·6. $C_{14}H_{17}ON$ requires C, 78·1; H, 8·0; N, 6·5%).

(b) *From* 2-(1-*ethylpropyl*)-8-*methoxyquinoline*-4-*carboxylic acid*. It proved impossible to decarboxylate the methoxy-acid (I; R = $CHEt_2$, R′ = CO_2H, R″ = Me) by heating it in boiling diphenyl or quinoline, or with Adkins, Burgoyne, and Scheider's decarboxylation catalyst,[5] and it sublimed unchanged when heated in an oil-bath under a high vacuum. The acid (3·5 g.) was therefore heated at atmospheric pressure in a Wood's-metal bath to a temperature well above its m. p. Carbon dioxide was evolved and a pale yellow oil distilled (2·7 g.). Since the distillate did not crystallise it was demethylated without purification by being heated under reflux for 4 hr. with constant-boiling hydrobromic acid (20 ml.). After being cooled the clear solution was nearly neutralised with 2N-sodium hydroxide, and the oil which separated was removed and distilled in steam. Crude 2-(1-ethylpropyl)-8-hydroxyquinoline which separated in the aqueous distillate was collected, taken up in dilute aqueous sodium hydroxide, and reprecipitated with acetic acid. After recrystallisation from methanol it gave a colourless product, m. p. 46°, which did not depress the m. p. of the previous specimen.

When this preparation was repeated on a larger scale, the final product (10 g.; b. p. 172—174°/9 mm.) showed great reluctance to recrystallise. The demethylation stage was therefore repeated, 1·5 g. of the desired product being readily obtained. The remaining oil (7·3 g.) was then treated with picric acid (8·2 g.) in the minimum volume of hot ethanol. After repeated crystallisation from boiling ethanol the *picrate* of 2-(1-ethylpropyl)-8-hydroxyquinoline was obtained as yellow needles (5·3 g.), m. p. 187° (Found: N, 24·2. $C_{14}H_{17}ON,C_6H_3O_7N_3$ requires N, 24·0).

Sensitivity Tests.—The procedure already described [1,4] was adopted, but in measurements with 2-(1-ethylpropyl)oxine it was necessary to use 50% v/v aqueous ethanol in place of water when making up the test solution to the constant volume of 6·2 ml.

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[*Received, June 17th*, 1958.]

[5] Adkins, Burgoyne, and Schneider, *J. Amer. Chem. Soc.*, 1932, **54**, 1138.

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50. *The Stability of Iron Complexes. Part III.*[1] *A Comparison of* 1 : 1 *Ferric and Ferrous Amino-acid Complexes.*

By D. D. PERRIN.

The stability constants of twenty 1 : 1 ferrous complexes with α-amino-acids were obtained in water at 20° and $I = 1$, in a medium consisting essentially of potassium chloride, by potentiometric titration. The constants vary with the proton, acid, dissociation constants of the amino-acids, but to a much smaller extent than for the corresponding ferric complexes. Molar electrode potentials for the Fe^{3+} : Fe^{2+} amino-acid complexes, calculated from these results, are linearly related to the logarithms of the dissociation constants of the amino-acids. The slope of the line is probably somewhat greater than similar slopes for the iron 1 : 1 polyaza-1-naphthol and 5-substituted 1 : 10-phenanthroline complexes.

LITTLE quantitative information exists on the relative stabilities in aqueous solutions of ferric and ferrous complexes with a series of similar ligands. Albert and Hampton [2] obtained stability constants of 1 : 1 ferric and ferrous complexes with seven polyaza-1-naphthols (" aza-oxines ") and Smith and Richter [3] measured the oxidation–reduction

[1] Parts I and II, *J.*, 1958, 3120, 3125.
[2] Albert and Hampton, *J.*, 1954, 505.
[3] Smith and Richter, *Ind. Eng. Chem. Anal.*, 1944, **16**, 580.

potentials of iron chelates of four substituted 1 : 10-phenanthrolines. Although stability constants for both ferric and ferrous iron with a further eighteen organic ligands have been tabulated,[4] the ligands were of so many different types, and experimental conditions varied so widely, that few quantitative comparisons are possible. Qualitatively, as is to be expected from entropy effects [5] and electrostatic considerations, ferric complexes are more stable than ferrous complexes when the ligand is an anion; the relative stability appears to increase with the charge on the ligand. In the few cases so far studied where the ligand is a neutral molecule the ferrous complexes are the more stable.

The dissociation constant, K', of the ligand is also important. In many cases, including the 1 : 1 ferric–amino-acid complexes,[1] the stability constants of a cation with a series of similar ligands follow approximately the relation [6] $\log K = \alpha pK' + c$, where α and c are constants. It has been suggested that this relation is somewhat fortuitous and is obeyed so widely only because most ligands are at the same time both π- and σ-electron donors (or acceptors).[7] Although the value of α appears to increase with the electronegativity of the cation, from about 0·3 for Ag^+ in complexes with secondary amines [8] to 1·7 for Fe^{3+} in amino-acid complexes,[1] factors affecting α have not been studied in detail. It has also been suggested that from thermodynamic reasoning α should be unity; [9] on the other hand it has been stated that there is no reason to expect this value.[5] From a simple electrostatic model α should increase with increasing cationic charge and decreasing distance of separation of the cation and ligand.[7] The effect of the dissociation constants of similar ligands on the relative stabilities of ferric and ferrous complexes, and hence on their standard oxidation–reduction potentials, has been very little studied, except that it has been observed that the potentials of iron complexes of 5-substituted 1 : 10-phenanthrolines varied with pK' of the corresponding *para*-substituted benzoic acids [10] and of the ligands themselves.[11] Such a study has recently been commenced in mixed aqueous organic solvents.[12]

The results now reported for 1 : 1 ferrous complexes with α-amino-acids are part of an investigation of the effects of the charge and the dissociation constant of a ligand on the stability in aqueous solution of its ferric and ferrous complexes. Amino-acids are convenient complex-forming species for this purpose because the stability constants of the corresponding ferric complexes are known. However, although stability constants of many 1 : 2 ferrous–amino-acid complexes have been recorded,[4] values for the 1 : 1 ferrous complexes have been published only for glycine,[13] glutamic acid,[13] lysine,[14] cysteine,[14] arginine,[14] and ornithine.[14]

Experimental

The amino-acids were of the same quality as in Part II. All other reagents were of analytical grade. Ferrous perchlorate solutions were prepared by double decomposition of carefully neutralised barium perchlorate and ferrous sulphate solutions. Ferric ion was removed by passage through a column of the ferrous salt of a cation-exchange resin (Amberlite IR-120). The eluates, which gave only weak tests for ferric ion on addition of sodium thiocyanate, were stored under nitrogen. Ferrous concentrations were determined by titration

[4] Bjerrum, Schwarzenbach, and Sillén, "Stability Constants. Part 1: Organic Ligands," The Chemical Society, London, Spec. Publ. No. 6, 1957.
[5] Williams, in "Special Lectures in Biochemistry, 1954—1955," University College, London, p. 43.
[6] Keller and Parry, in "The Chemistry of the Co-ordination Compounds," ed. Bailar, Chapman and Hall, London, 1956, p. 180.
[7] Jones, Poole, Tomkinson, and Williams, *J.*, 1958, 2001.
[8] Bjerrum, *Chem. Rev.*, 1950, **46**, 381.
[9] Irving and Rosotti, *J.*, 1954, 2910.
[10] Ewens, *Nature*, 1945, **155**, 398.
[11] Brandt and Gullstrom, *J. Amer. Chem. Soc.*, 1952, **74**, 3532.
[12] Tomkinson and Williams, *J.*, 1958, 2010.
[13] Albert, *Biochem. J.*, 1953, **54**, 646.
[14] *Idem, ibid.*, 1952, **50**, 690.

with potassium dichromate in phosphoric acid, sodium diphenylamine-4-sulphonate being used as indicator.

Stability constants of the 1 : 1 ferrous–amino-acid complexes were obtained potentiometrically by Bjerrum's method [15] as developed by Calvin and Wilson,[16] by use of the relationship,

$$K_1 = \frac{\bar{n}}{(1-\bar{n})[L^-]} - K_2\left(\frac{2-\bar{n}}{1-\bar{n}}\right)[L^-] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (i)$$

where K_2 is the overall stability constant of the 1 : 2 metal–amino-acid complex. The rigorous graphical treatment of eqn. (i) described by Irving and Rossotti (*J.*, 1953, 3397) could not be used to evaluate K_1 accurately because over the selected range of $\bar{n}$ values (0·06—0·40), the quantity, $\bar{n}/\{(1-\bar{n})[L^-]\} - K_1$, was too sensitive to experimental error for an estimate of K_2 to be obtained. Thus for all values of $\bar{n} \leqslant 0{\cdot}20$, the range $K_1/K_2 = 10$ to $K_1/K_2 = \infty$ is covered by a difference of less than 0·03 log unit, which is about half the experimental error of a single estimate of log K_1; even at $\bar{n} = 0{\cdot}40$ the difference is less than 0·08 log unit. Accordingly, the approximation [17]

$$\log K_2 = 2 \log K_1 - 1 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (ii)$$

was used in evaluating the final, small, term in eqn. (i). Table 1 gives experimental results for the complexes studied. Values of log K_1 have been calculated on the assumption that complex formation takes place through the uncharged α-amino-nitrogen atom of the amino-acid anion. Probably in the compound so formed the ferrous ion is chelated between the α-amino-nitrogen and one or more of the carboxylic oxygen atoms.[14, 17, 18] However, because the carboxyl groups are already fully ionised under the experimental conditions, any bonding to them is not detected potentiometrically. Solutions 0·0100M in amino-acid and 0·0050M in ferrous ion were titrated, under nitrogen, with 0·1M-potassium hydroxide (carbonate free). A stream of nitrogen, free from oxygen and saturated with water vapour, was used for mixing the solutions. All measurements were made at 20° ± 0·1°, with a Cambridge bench model pH meter and a glass electrode–saturated calomel electrode assembly. A constant ionic strength of 1·0 was maintained by adding potassium chloride. Sodium perchlorate, which was used for this purpose in studying ferric complex formation (Part II), was not satisfactory for the present investigation because, in the near-neutral solutions, it oxidised ferrous ion. From the similarity of the activity coefficients of hydrochloric acid in sodium perchlorate and potassium chloride solutions [19] it was assumed that these salts are comparable in their effects on the stability constants of the iron–amino-acid complexes.

For the amino-acids studied, ferrous and ferric complexes are believed to be structurally similar.[1] Hence, from the equation,

$$E_L^\circ = E^\circ_{Fe^{3+},\,Fe^{2+}} - 2{\cdot}3026\,(\boldsymbol{R}T/\boldsymbol{F})\,(\log K_{Fe^{3+}} - \log K_{Fe^{2+}}) \quad . \quad . \quad . \quad (iii)$$

the standard oxidation–reduction potential, E_L°, of any corresponding pair of 1 : 1-iron–amino-acid complexes can be calculated once the stability constants, $K_{Fe^{3+}}$ and $K_{Fe^{2+}}$, of the ferric and the ferrous complexes are known. At 20° the standard potential of the ferric–ferrous electrode, in a sodium perchlorate solution of unit ionic strength, was 0·4956 v against a saturated calomel electrode, an ammonium nitrate–sodium nitrate–agar bridge being used. Taking $E_{sat.\,calc.}$ as 0·244 v at 20°,[20] we get $E^\circ_{Fe^{3+},\,Fe^{2+}} = 0{\cdot}740$ v at 20° and $I = 1$, in good agreement with the figure [21] of 0·741 v at 25°. Values of E_L° for 1 : 1 iron–amino-acid complexes, calculated from eqn. (iii) by using data [1] for the ferric complexes and the present results for the ferrous complexes, are given in Table 2.

[15] Bjerrum, "Metal Ammine Formation in Aqueous Solution," P. Haase and Son, Copenhagen, 1941.
[16] Calvin and Wilson, *J. Amer. Chem. Soc.*, 1945, **67**, 2003.
[17] Albert, *Biochem. J.*, 1950, **47**, 531.
[18] Flood and Lorås, *Tidsskr. Kjemi Bergvesen Met.*, 1945, **5**, 83; Maley and Mellor, *Nature*, 1950, **165**, 453.
[19] Hawkins, *J. Amer. Chem. Soc.*, 1932, **54**, 4480; Bates and Urmston, *ibid.*, 1953, **55**, 4068.
[20] Ewing, *J. Amer. Chem. Soc.*, 1925, **47**, 301; Chateau, *J. Chim. phys.*, 1954, **51**, 590.
[21] Schumb, Sherrill, and Sweetser, *J. Amer. Chem. Soc.*, 1937, **59**, 2360.

TABLE 1. *Derivation of stability constants for* 1 : 1 *ferrous–amino-acid complex.*

$[Fe^{2+}]$ = 0·005M, [HL] = 0·01M, I = 1M (KCl)

$\bar{n}$ =	0·06	0·08	0·10	0·12	0·16	0·20	0·24	0·30	0·40	0·50
(*a*) Glycine.										
pH	—	6·80	6·95	7·08	7·24	7·38	7·48	7·62	7·80	—
$-\log [L^-]$	—	4·980	4·835	4·710	4·560	4·430	4·341	4·217	4·065	—
$\log K_1$	—	3·91	3·87	3·83	3·82	3·80	3·80	3·80	3·81	—
(*b*) Alanine.										
pH	—	7·08	7·26	7·40	7·58	7·72	7·80	7·89	8·00	—
$-\log [L^-]$	—	4·730	4·555	4·420	4·250	4·120	4·051	3·977	3·896	—
$\log K_1$	—	(3·66)	3·59	3·54	3·51	3·48	3·52	3·57	(3·68)	—
(*c*) α-Amino-*n*-butyric acid.										
pH	—	7·20	7·34	7·44	7·60	7·74	7·83	7·95	8·10	—
$-\log [L^-]$	—	4·480	4·345	4·250	4·100	3·970	3·891	3·787	3·656	—
$\log K_1$	—	3·41	3·38	3·37	3·36	3·34	3·36	3·38	3·43	—
(*d*) α-Amino*iso*butyric acid.										
pH	7·38	7·61	7·72	7·81	7·88	7·96	—	8·06	8·15	—
$-\log [L]^-$	4·725	4·500	4·395	4·305	4·250	4·180	—	4·107	4·046	—
$\log K_1$	3·52	3·43	3·42	3·42	3·51	3·56	—	(3·72)	(3·85)	—
(*e*) Valine.										
pH	6·95	7·14	7·30	7·39	7·55	7·68	—	7·87	8·02	—
$-\log [L^-]$	4·655	4·470	4·315	4·230	4·080	3·960	—	3·797	3·676	—
$\log K_1$	3·46	3·40	3·37	3·35	3·34	3·34	—	3·39	3·46	—
(*f*) Leucine.										
pH	6·96	7·16	7·28	7·37	7·52	7·63	—	7·86	7·96	—
$-\log [L^-]$	4·675	4·480	4·365	4·280	4·140	4·040	—	3·837	3·766	—
$\log K_1$	3·48	3·41	3·40	3·40	3·40	3·42	—	3·43	(3·56)	—
(*g*) β-Phenylalanine										
pH	—	6·78	6·96	7·08	7·24	7·36	7·48	7·60	7·77	—
$-\log [L^-]$	—	4·420	4·215	4·130	3·980	3·870	3·761	3·657	3·516	—
$\log K_1$	—	3·35	3·25	3·25	3·24	3·24	3·23	3·25	3·28	—
(*h*) Serine.										
pH	6·44	6·62	6·74	6·86	7·02	7·15	—	7·39	7·56	—
$-\log [L^-]$	4·695	4·520	4·405	4·290	4·140	4·020	—	3·807	3·666	—
$\log K_1$	3·50	3·45	3·44	3·41	3·40	3·39	—	3·40	3·43	—
(*i*) Threonine.										
pH	6·31	6·50	6·63	6·73	6·88	7·00	—	7·25	7·42	—
$-\log [L^-]$	4·565	4·375	4·255	4·160	4·020	3·910	—	3·687	3·546	—
$\log K_1$	3·37	3·31	3·29	3·28	3·28	3·28	—	3·28	3·31	—
(*j*) Aspartic acid.										
pH	6·08	6·20	—	6·38	6·54	6·66	—	6·92	7·12	7·30
$-\log [L^-]$	5·524	5·409	—	5·239	5·089	4·979	—	4·746	4·575	4·413
$\log K_1$	4·32	4·34	—	4·36	4·35	4·35	—	4·33	4·33	4·31
(*k*) Glutamic acid.										
pH	6·78	6·97	—	7·20	7·34	7·47	—	7·70	7·86	—
$-\log [L^-]$	4·775	4·590	—	4·370	4·240	4·120	—	3·917	3·786	—
$\log K_1$	3·58	3·52	—	3·49	3·50	3·49	—	3·51	3·56	—
(*l*) Asparagine.										
pH	—	6·26	6·40	6·52	6·69	6·84	6·95	7·10	7·30	—
$-\log [L^-]$	—	4·550	4·415	4·300	4·140	4·000	3·901	3·767	3·596	—
$\log K_1$	—	3·48	3·45	3·42	3·40	3·37	3·37	3·35	3·34	—
(*m*) Arginine.										
pH	6·70	6·90	—	7·15	7·32	7·44	—	7·68	7·82	—
$-\log [L^-]$	4·525	4·330	—	4·090	3·930	3·820	—	3·607	3·496	—
$\log K_1$	(3·33)	3·26	—	3·21	3·19	3·19	—	3·20	3·27	—
(*n*) Ornithine.										
pH	6·48	6·75	6·88	6·98	7·17	7·29	—	7·53	7·70	—
$-\log [L^-]$	4·465	4·200	4·075	3·980	3·800	3·690	—	3·477	3·336	—
$\log K_1$	(3·27)	3·13	3·11	3·10	3·10	3·06	—	3·06	3·10	—
(*o*) Proline.										
pH	7·20	7·42	7·57	7·66	7·76	7·82	—	7·96	8·05	—
$-\log [L^-]$	5·335	5·220	4·975	4·890	4·800	4·750	—	4·637	4·576	—
$\log K_1$	4·14	4·05	4·01	4·01	4·06	4·13	—	(4·25)	(4·38)	—

TABLE 1. (*Continued.*)

$\bar{n}$ =	0·06	0·08	0·10	0·12	0·16	0·20	0·24	0·30	0·40	0·50
(*p*) Hydroxyproline.										
pH	6·41	6·60	6·70	6·80	6·96	7·08	—	7·32	7·50	—
$-\log [L^-]$	5·185	5·000	4·905	4·810	4·660	4·550	—	4·337	4·186	—
$\log K_1$	3·99	3·93	3·94	3·93	3·92	3·92	—	3·93	3·95	—
(*q*) Tryptophan.										
pH	6·77	6·95	7·10	7·20	7·35	7·47	—	7·68	7·84	—
$-\log [L^-]$	4·686	4·511	4·366	4·271	4·131	4·021	—	3·838	3·707	—
$\log K_1$	3·49	3·44	3·40	3·39	3·39	3·40	—	3·44	3·50	—
(*r*) Methionine.										
pH	6·64	6·84	6·98	7·07	7·24	7·36	—	7·58	7·75	—
$-\log [L^-]$	4·516	4·321	4·186	4·101	3·941	3·831	—	3·638	3·497	—
$\log K_1$	3·32	3·25	3·22	3·22	3·20	3·20	—	3·23	3·27	—
(*s*) Sarcosine.										
pH	7·18	7·42	7·56	7·68	7·82	7·90	—	8·02	8·08	—
$-\log [L^-]$	4·855	4·620	4·485	4·370	4·240	4·170	—	4·077	4·046	—
$\log K_1$	(3·66)	3·55	3·52	3·49	3·50	3·55	—	(3·69)	(3·86)	—
(*t*) Glycylglycine.										
pH	6·29	6·52	6·64	6·76	6·94	7·07	—	7·30	7·46	—
$-\log [L^-]$	3·955	3·730	3·615	3·500	3·330	3·210	—	3·007	2·876	—
$\log K_1$	(2·76)	2·66	2·65	2·62	2·59	2·58	—	2·60	2·65	—

Figures in parentheses have been omitted in obtaining average values.

TABLE 2. *Stability constants of* 1 : 1 *ferrous–amino-acid complexes, and molar electrode-potentials of ferric–ferrous couples.*

(In water at 20° and unit ionic strength of potassium chloride.)

Amino-acid	pK' (Ref. 1) (α-NH_2)	log K_1	$E_L°$ (v)	Amino-acid	pK' (Ref. 1) (α-NH_2)	log K_1	$E_L°$ (v)
Glycine	9·76	3·83	0·380	Glutamic acid	9·54	3·52	0·240
Alanine	9·79	3·54	0·340	Asparagine	8·79	3·40	0·440
α-Amino-*n*-butyric acid	9·66	3·37	0·370	Arginine	9·21	3·22	0·420
α-Amino*iso*butyric acid	10·09	3·48	0·345	Ornithine	8·93	3·09	0·415
Valine	9·59	3·39	0·380	Proline	10·52	4·07	0·395
Leucine	9·62	3·42	0·362	Hydroxyproline	9·58	3·94	0·445
β-Phenylalanine	9·18	3·26	0·415	Tryptophan	9·43	3·43	0·415
Serine	9·12	3·43	0·405	Methionine	9·13	3·24	0·400
Threonine	8·86	3·30	0·430	Sarcosine	10·02	3·52	0·380
Aspartic acid	9·56	4·34	0·330	Glycylglycine	8·23	2·62	0·360

DISCUSSION

The approximation (ii) provides a rough check on the results if it is assumed that the effect of ionic strength on the stability constants is the same for all amino-acids. From results for glycine (present work and ref. 12) this effect is found to be a decrease of about 0·5 in log K_1 as I increases from 0·01 to 1·0 (KCl). For eight of the ten amino-acids where such a comparison is possible,[14,17] estimated and observed values of log K_1 do not differ by more than 0·1; only for tryptophan (0·37) is the difference greater than 0·2. On the other hand, previous values [14] for the 1 : 1 ferrous complexes with ornithine and glutamic acid are much higher than were found in the present work (which now places the ferrous–ornithine complex in its correct position in the Irving–Williams [22] series).

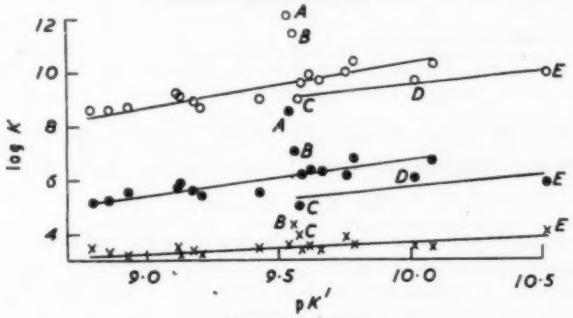
From the Figure the complex-forming ability of an amino-acid with ferrous ion varies much less with the proton, acid, dissociation constant of the amino-acid than was found for ferric ion. In both cases, however, approximately linear relationships are obtained. For the ferrous complexes the slope, α, of the line drawn by the method of least squares is about 0·4. Although subject to considerable uncertainty because of the scatter of the experimental points, values of α of this order of magnitude for the 1 : 1 copper and zinc

[22] Irving and Williams, *Nature*, 1948, **162**, 746.

amino-acid complexes are obtained from published [14,17,23] data if the approximation (ii) is assumed. On the other hand, for the corresponding ferric complexes, α is about 1·7.

The ferrous–aspartic acid complex is more stable than would be predicted from its dissociation constant, probably indicating additional chelation through the β-carboxyl group. The increase in stability is less than for the ferric complex, possibly because of the difference in the charges on the metal ions. The lower charge, and the requirement that the ring formed must be seven-membered, may explain why enhanced stability is not observed for the ferrous–glutamic acid complex. Similarly, and unlike the ferric complex, 1 : 1 ferrous–glycylglycine is less stable than predicted from the dissociation constant of glycylglycine. In contrast to the ferric complexes, the 1 : 1 ferrous–proline and –hydroxyproline complexes are somewhat more stable than expected.

Dependence of stability constants and oxidation–reduction potentials of iron complexes on dissociation constants of amino-acids.



Anomalous acids:

A, glutamic acid. *B*, aspartic acid. *C*, hydroxyproline. *D*, sarcosine. *E*, proline.

○ log $K_{Fe^{3+}}$ (ref. 1). ● log $K_{Fe^{3+}}$ − log $K_{Fe^{2+}}$. × log $K_{Fe^{2+}}$.

The difference of 1·3 between $\alpha_{Fe^{3+}}$ and $\alpha_{Fe^{2+}}$ for the 1 : 1 amino-acid complexes gives directly from eqn. (iii) their change of standard oxidation–reduction potential with dissociation constant as −0·075 volt/pK' unit. The basic skeleton, –N·C·C·O–, of the amino-acid chelating system is also found in oxine (8-hydroxyquinoline) and its aza-derivatives. However, probably because of large individual variations in resonance energies of the ligands as different ring carbon atoms are replaced by nitrogen, the stability constants of neither the 1 : 1 ferric nor the 1 : 1 ferrous series comprising 8-hydroxyquinoline,[2,13] 8-hydroxyquinoline-5-sulphonic acid,[2,13] and polyaza-1-naphthol [2] complexes show much correlation with dissociation constants. On the other hand, the difference, log $K_{Fe^{3+}}$ − log $K_{Fe^{2+}}$, is roughly linear with pK' and of slope about 0·8, giving $dE_L°/d(pK') \sim -0·045$ v. From recent measurements,[12] the plot of oxidation–reduction potentials of 1 : 3 iron complexes of substituted 8-hydroxyquinolines in 50% dioxan–water against pK' (pK_{OH}) gives a straight line with a slope, $dE_L°/d(pK')$, $\sim -0·080$ v; except for 5-cyano-8-hydroxyquinoline ($\delta \sim 0·12$ v) the deviation, δ, of points from this line averages 30 mv. However, if potentials are plotted against the sum, pK_{NH} + pK_{OH}, which has been suggested as a measure of ligand basicity,[7] no simple relation is found.[12] If the factors governing the binding of protons and cations are similar, it seems reasonable to expect that the stability constants of metal chelates might depend on the dissociation constant of the more strongly proton-binding of the two chelating groups. Hence, for the substituted 8-hydroxyquinolines where pK_{OH} is 5—8 log units greater than pK_{NH}, pK_{OH} rather than pK_{NH} + pK_{OH} should be used in comparing the observed oxidation–reduction potentials. If this

[23] Perkins, *Biochem. J.*, 1954, **57**, 702; Monk, *Trans. Faraday Soc.*, 1951, **47**, 292, 297.

is done, 5-formyl- and 5-cyano-8-hydroxyquinoline complexes are found to have potentials much nearer the predicted values than if the comparison uses the sums of the pK values. Similarly, if an error of about 10 mv is assumed, the oxidation–reduction potentials of five 1 : 3 iron–substituted phenanthroline complexes (probably in dioxan–water) [12] are linear with pK_{NH}. Results for some 1 : 3 iron complexes of 5-substituted 1 : 10-phenanthrolines in M-sulphuric acid [3,11] show $E_L°$ to vary directly with pK', within experimental uncertainty, giving $dE_L°/d(pK') = -0{\cdot}120$ v. If it is assumed that, because the ligands are neutral molecules, the pK' effect is roughly the same for successive complex formation, $dE_L°/d(pK')$ for the corresponding 1 : 1 complexes thus becomes of the order of $-0{\cdot}040$ v. For all three groups (amino-acid, 8-hydroxyquinoline, and phenanthroline) of 1 : 1 iron complexes in aqueous solution it appears, therefore, that as the basic strength of the ligand is increased the firmness with which the valency electron is bound to ferrous ion varies in approximately the same manner. Whether this is also true of ligands containing other skeletons, such as –O·C·C·C·O–, is at present being examined.

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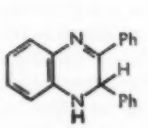
51. *The Effect of Acid on the Electronic Spectra of Organic Molecules containing Conjugated and Unconjugated Nitrogen Atoms.*

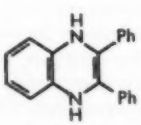
By J. N. MURRELL.

The effect of acid on the electronic spectra of organic molecules containing a conjugated and an unconjugated nitrogen atom bears little relationship to the possibility of writing structures in which the positive charge resonates between the two nitrogen atoms. A molecular-orbital theory of the charge-transfer character of the lowest excited states gives a better interpretation of the experimental results.

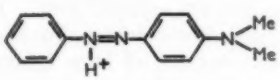
THE yellow solution of a dihydro-2 : 3-diphenylquinoxaline instantaneously becomes deep red in the presence of dilute acid.[1] The change is reversed on neutralizing the solution. An explanation of this phenomenon was sought, to decide between the two most likely structures for this compound, (I) and (II).



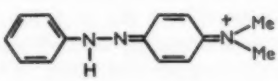
(I)



(II)



(III)

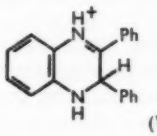


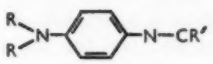
(IV)

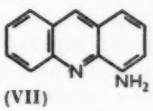
The colour of the free base favours (I), because amino-substituted anils are yellow whereas 9 : 10-dihydrophenazine is colourless. However, if (I) is adopted and assumed to be protonated on the conjugated nitrogen atom, then from conventional valence-bond or resonance ideas there is no reason to expect a large red shift in its absorption spectrum on acidification. Valence-bond theory would associate a red shift with the introduction of new, or lower-energy, resonance structures. For example, *p*-dimethylaminoazobenzene changes from yellow to red on acidification. The protonated form is assumed to be (III) but with a strong contribution from the structure (IV). The red colour is presumably associated with a transition from the ground state (mainly III) to an excited state (mainly IV). Such resonance is possible only when the two nitrogen atoms are separated by an odd number of conjugated atoms. In (I), the two nitrogen atoms are separated by an

[1] Fischer, *Ber.*, 1891, **24**, 719.

even number of conjugated atoms, hence the only low-energy valence structure that can be written is (V).


(V)


(VI)

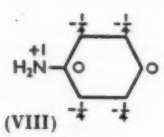

(VII)

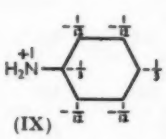
The behaviour of the dihydroquinoxaline is not an isolated case. A yellow-to-red colour change is observed on acidifying [2] *p*-amino-substituted anils of type (VI), and 1-aminoacridine (VII) changes from yellow to blue-black.[3] In neither case can the positive charge " resonate " between the two nitrogen atoms.

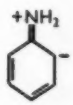
Since the resonance theory appears to fail in these cases, let us consider the molecular-orbital representation. The first absorption bands in amino-aromatic molecules probably have a considerable amount of charge-transfer character, the NH_2 group being a strong electron donor. For example, in aniline there are two low-lying vacant benzene molecular orbitals which can accept an electron from the NH_2 group, one symmetric and one antisymmetric to a rotation of 180° about the C–N axis. The charge densities associated with these two states, relative to the ground state, are depicted in (VIII) and (IX).

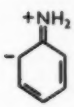
If we could attach a proton to the aromatic ring of the aniline molecule, we would predict that (VIII) would be stabilized if the proton were in the *ortho*- or the *meta*-position but not if it were in the *para*-position, and (IX) would be stabilized four times as much in the *para*-position as in the *ortho* or *meta*.

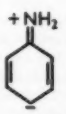
The valence-bond charge-transfer states however will be some combination of the structures (X), (XI), and (XII). The state which is antisymmetric to rotation about the C–N bond will be $\sqrt{\frac{1}{2}}(X - XI)$, and that which is symmetric will be some mixture of


(VIII)


(IX)


(X)


(XI)


(XII)

$\sqrt{\frac{1}{2}}(X + XI)$ and (XII). Thus, the donated charge appears either in the *ortho*- or the *para*-position but not in the *meta*. We should therefore expect no appreciable red shift on attaching a proton to the *meta*-position.

TABLE 1. *Wavelengths of the first two absorption bands of the aminopyridines in neutral (n) and acid (a) solution.*

	Aniline [a]	2-Aminopyridine [b]	3-Aminopyridine [b]	4-Aminopyridine [b]
λ_n (mμ)	288, 235	295, 234	300, 240	270,* 244
λ_a (mμ)	—	300, 227	317, 250	262
$-\Delta\nu$ (cm.$^{-1}$)	—	600, −1300	1800, 1700	~0, 2800

* Shoulder. [a] Klevens and Platt, *J. Amer. Chem. Soc.*, 1949, **71**, 1714. [b] Steck and Ewing, *ibid.*, 1948, **70**, 3399.

Calculations show that the lowest excited state of aniline is antisymmetric with respect to the two-fold axis (although the lowest energy charge-transfer configuration is in fact the symmetric one), whilst there is a state of slightly higher energy which is symmetric.[4] Table 1 gives the wavelengths of the first two absorption bands of the amino-pyridines

[2] Moore and Woodbridge, *J. Amer. Chem. Soc.*, 1908, **30**, 1001.
[3] Matsumara, *ibid.*, 1939, **61**, 2247.
[4] Murrell, *Proc. Phys. Soc.*, 1955, *A*, **68**, 969.

in ethanol, and in ethanol with acid added to pH 2: in these circumstances the heterocyclic nitrogen atom will be protonated. The wavelengths of the corresponding bands of aniline are given for comparison; they undergo a blue shift in acid owing to protonation of the amino-group.

For the band of lower energy, there is a red shift of 600 cm.$^{-1}$ and 1800 cm.$^{-1}$ for the 2- and 3-amino-compounds respectively, and for the 4-aminopyridine no shift can be detected as it is obscured by the more intense upper band: however, we probably could have detected a red shift larger than 500 cm.$^{-1}$. The upper band undergoes a red shift of 1700 cm.$^{-1}$ and 2800 cm.$^{-1}$ in the case of the 3- and 4-amino-pyridines respectively, but a blue shift of 1300 cm.$^{-1}$ in the 2-amino-compound. The latter, unexpected from either the molecular-orbital or the valence-bond viewpoint, may be due to second-order energy changes, or to the close proximity of the NH_2 group to the heterocyclic atom. In general, however, we can say from the evidence on 3-aminopyridine that molecular-orbital theory gives a rather better picture of any charge transfer in the excited states of the amino-pyridines than does resonance theory.

The amino *N*-heterocyclic compounds derived from naphthalene provide a more extensive set of data to test resonance theory than is available from the pyridines. Table 2 gives the wavelength of the first absorption band for some amino-quinolines, -*iso*-quinolines, and -quinazolines in neutral and acid solution. In the discussion which follows it is assumed that the molecules are protonated on the heterocyclic nitrogen atoms. For quinazoline I make no attempt to decide whether the proton goes to the 1- or the 3-position; the following arguments hold whichever is the case. R denotes those molecules for which resonance theory would predict a large red shift on acidification.

Table 2 shows that there is little connection between the " resonance " cases and a

TABLE 2. *Wavelengths of the first absorption band of some amino-*N*-heterocyclic compounds of the naphthalene series.*

		λ_a (mμ)	λ_a (mμ)	$-\Delta\nu$ (cm.$^{-1}$)
α-Naphthylamine		322		
4-Aminoquinoline	R	305 + 315 *	305 + 315	0
5-Aminoquinoline	R	345	418	5060
8-Aminoquinoline		338	388	3810
1-Amino*iso*quinoline	R	332 + 300	330 + 280	−180, −2380
4-Amino*iso*quinoline		332	354	1870
5-Amino*iso*quinoline		332	378 + 340	3660 (or 710)
8-Amino*iso*quinoline		345 + 307	417 + 325	5000, 1800
4-Aminoquinazoline	R	323 + 312	324 + 311	100
5-Aminoquinazoline	R	372 + 336 †	462 + 305	5230, −3020
8-Aminoquinazoline		338	415	5490
β-Naphthylamine		340		
2-Aminoquinoline	R	315	308	−720
3-Aminoquinoline		350	372	1690
6-Aminoquinoline		352	383	2300
7-Aminoquinoline	R	352	390	2770
3-Amino*iso*quinoline	R	353	390	2690
6-Amino*iso*quinoline	R	326	352 + 337	2270 (or 1000)
7-Amino*iso*quinoline		349	385	2680
2-Aminoquinazoline	R	352	348 + 339 †	−320 (or −1090)
6-Aminoquinazoline		360	310 *	−4480
7-Aminoquinazoline	R	345	373	2180

* Inflexion. † Shoulder.

Data on aminoquinolines are from ref. *a* of Table 1, and for amino*iso*quinolines and quinazolines from ref. 15.

red shift on acidification. For example, the bands of 2- and 4-aminoquinoline, 1-amino-*iso*quinoline, and 2- and 4-aminoquinazoline are shifted, if anything, slightly towards the blue, whereas 8-aminoquinazoline, a non-resonance case, shows the largest red shift of all.

Let us compare the 5- and 8-amino-compounds. On resonance theory the absorption band of one of these should undergo a large red shift on acidification, and the other should

not be shifted significantly. On molecular-orbital theory, however, the 5- and 8-amino-compounds should be shifted by the same amount, the electron from the amino-group going into an orbital which, by symmetry, gives rise to the same electron density at the two positions. From the Table, the molecular-orbital theory is evidently more satisfactory, although there is some sympathy for the resonance theory for quinoline and *iso*quinoline. The 6- and 7-amino-compounds show a similar behaviour, and support the molecular-orbital theory, although 6-aminoquinazoline is exceptional on either theory; Osborne and Schofield [5] suggest that it is protonated on the amino-group but, as they suggest, the molecule needs further examination.

It has been assumed here that the shifts in the absorption bands which occur on acidification of amino-*N*-heterocyclic compounds can be interpreted by a first-order perturbation theory; that is, that the shifts depend only on the difference in the electron density on the heterocyclic atom between the ground and the excited state. If there is no charge transfer character in the excited state, then the energy changes would have to be interpreted by a second-order perturbation theory.[6] Calculations show that the lowest excited state of aniline has only about 17% of charge-transfer character associated with the structure (VIII). However, since second-order energy changes are usually rather small, the first-order treatment given in this paper will probably still be applicable.

It remains to be said that both molecular-orbital and valence-bond wave functions are only attempts to obtain a first approximation to the true wave function of a molecule. If molecular-orbital theory is extended by configurational interaction, it will take on some of the properties of the valence-bond functions. If the valence-bond functions are extended in a similar way they become more like the molecular-orbital functions. The best functions lie somewhere between the two, but the evidence now presented suggests that any charge-transfer character in the lowest excited states of amino-*N*-heterocyclic compounds is more closely represented by the molecular-orbital than by the valence-bond functions.

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[5] Osborne and Schofield, *J.*, 1956, 4191.
[6] Murrell, *J. Mol. Phys.*, 1958, **1**, 384.

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52. *Exchange Studies of Certain Chelate Compounds of the Transitional Metals. Part VI.* The Cobalt(II)–Phenanthroline System.*

By PETER ELLIS and R. G. WILKINS.

The rate constants for dissociation of $[Co\ phen_3]^{3+}$ and $[Co\ phen]^{3+}$ have been determined from exchange experiments involving [^{14}C]phenanthroline and $^{60}Co^{3+}$. The values obtained are, respectively, $1{\cdot}4 \times 10^{16}$ exp $(-20{,}600/\boldsymbol{RT})$ and $1{\cdot}6 \times 10^{14}$ exp $(-19{,}400/\boldsymbol{RT})$ min.$^{-1}$. The kinetic parameters are compared with those of analogous systems and, in particular, the energies of activation are explained in terms of the crystal field theory of co-ordinate bonding.

THE rates of dissociation of complexes of cobalt(II), unlike those of cobalt(III), are rapid at ordinary temperatures.[1] This is strikingly shown by the behaviour towards exchange of such complexes with " labelled " metal or ligand species.[2] Apart from certain quadridentate complexes of cobalt(II) in pyridine,[3] all exchange reactions of cobalt(II) complexes which have so far been examined are fast.

* Part V, *J.*, 1957, 4521.

[1] Taube, *Chem. Rev.*, 1952, **50**, 69.
[2] Stranks and Wilkins, *ibid.*, 1957, **57**, 743.
[3] West, *J.*, 1954, 395.

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The lability of cobalt(II)–phenanthroline complexes has been demonstrated in at least three different ways: (*a*) the ready development of a red colour (due to ferroin) when mono-, bis-, or tris-phenanthrolinecobalt(II) ions are added to ferrous ions in aqueous solution,[4] (*b*) the rapid exchange of $[Co\ phen_3]^{2+}$ with $^{60}Co^{2+}$ at 15° in aqueous solution [5] (two points we shall return to later), and (*c*) the ability of $[Co\ phen_3]^{2+}$ to catalyse the exchange of $[Co\ phen_3]^{3+}$ with [^{14}C]phenanthroline.[6] The processes involved in (*a*) and (*b*), although fast, can, however, be measured and in the present study the kinetics of dissociation of $[Co\ phen_3]^{2+}$ and $[Co\ phen]^{2+}$ * have been determined from measurement of exchange rates at 0—15°.

Experimental

Materials.—[^{14}C]Phenanthroline hydrate was prepared as described previously.[7] Radiochemically pure cobalt(II) nitrate solution was prepared from neutron-irradiated metallic cobalt. In the kinetic studies, " AnalaR " chemicals were used. The following complex compounds were prepared:

$[Co\ phen_2Cl_2],H_2O$.—Phenanthroline hydrate (0·36 g.), 0·2M-cobalt nitrate (3 c.c.), and 2M-hydrochloric acid (4 c.c.) were mixed and left in ice overnight; pink crystals separated. These were washed with a small amount of ice-cold water and dried over silica gel (Found: C, 56·3; H, 3·5; N, 11·2; Co, 11·8. $C_{24}H_{16}N_4Cl_2Co,H_2O$ requires C, 56·6; H, 3·6; N, 11·0; Co, 11·6%). The *complex* labelled with ^{60}Co was prepared with one-tenth of the above quantities.

$[Co\ phenCl_2]$ was prepared as described by Pfeiffer and Werdelmann [4] (Found: C, 46·7; H, 3·0; N, 9·1. Calc. for $C_{12}H_8N_2Cl_2Co$: C, 46·5; H, 2·6; N, 9·0%).

$[Co\ phen(H_2O)_4][C_{10}H_6(SO_3)_2],H_2O$ was precipitated when a saturated solution of disodium naphthalene-1 : 5-disulphonate was added to a solution containing the $[Co\ phen]^{2+}$ ion (Found: Co, 9·5. $C_{22}H_{14}O_6N_2S_2Co,5H_2O$ requires Co, 9·6%). The pinkish *hydrate* on drying (P_2O_5) at 80° *in vacuo*, was dehydrated to a purple *salt* which rapidly regained the pink colour in air (Found: Co, 11·35. $C_{22}H_{14}O_6N_2S_2Co$ requires Co, 11·2%).

Cobalt analysis of phenanthroline-containing complexes was conveniently carried out by adding an excess of EDTA in buffer to the complex in solution, extraction with benzene of the phenanthroline liberated, and estimation of the excess of EDTA by back-titration with standard zinc solution.[8]

Exchange Runs.—(a) $[Co\ phen_3]^{2+}$–phen *exchanges*. A mixture was usually prepared from 0·8 mmolar cobalt(II) nitrate and 5·2 mmolar phenanthroline, forming the tris-complex and free phenanthroline *in situ*. Boiled-out conductivity water was used and nitrogen passed through the solution during the whole of the experiment. Later work indicated that omission of these precautions did not markedly alter the exchange rate, although the pale yellow solution became brown within several hours in the presence of oxygen. Because of the rapidity of the exchange, each point on the exchange curve was obtained from a separate experiment and each exchange run consisted of at least six points. Exchange was initiated by adding a stock solution of [^{14}C]phenanthroline (2·0 c.c.) to the inactive mixture described above (12·5 c.c.) which had settled to the desired temperature, and was terminated by the rapid addition of concentrated sodium perchlorate solution, which precipitated $[Co\ phen_3](ClO_4)_2$ together with some phenanthroline perchlorate. The latter was removed by washing the mixture with absolute alcohol, and the residual complex was washed with ether and dried. This procedure reproducibly gave 10—15% zero-time exchange. In one run (No. 2), separation was effected by extracting the free phenanthroline by vigorous shaking with ice-cold chloroform and assaying it as $[Fe\ phen_3](ClO_4)_2$ and the unextracted $[Co\ phen_3]^{2+}$ as the insoluble perchlorate in a similar manner to that in the $[Ni\ phen_3]^{2+}$–phen exchanges.[9] The two procedures gave similar values for k_{exch}, based on the expected relationship $R = k_{exch}[Co\ phen_3^{2+}]$. The results of the short

* Probable co-ordinated water molecules are not considered in this and subsequent formulæ.

[4] Pfeiffer and Werdelmann, *Z. anorg. Chem.*, 1950, **261**, 197.
[5] West, *J.*, 1954, 578.
[6] Ellis, Wilkins, and Williams, *J.*, 1957, 4456.
[7] *Idem*, *J.*, 1956, 3975.
[8] Schwarzenbach, " Complexometric Titrations," transl. by Irving, Methuen, London, 1957.
[9] Wilkins and Williams, *J.*, 1957, 1763.

kinetic study are shown in Table 1. Separate experiments obviated possible photochemical catalysis. The estimated energy of activation was 20·6 ± 0·5 kcal. mole^{-1}.

TABLE 1. *Exchange of* [Co phen$_3$]$^{2+}$ *with phenanthroline.*

Run no.	Temp.	[Complex] (mmole l.$^{-1}$)	[phen] (mmole l.$^{-1}$)	$t_{\frac{1}{2}(\text{exch})}$ (sec.)	10^4R (sec.$^{-1}$ mole l.$^{-1}$)	10^3k (sec.$^{-1}$)
1	0·0°	1·63	2·81	93	13·3	8·2
2	0·0	0·80	2·76	140	6·4	8·0
3	6·6	0·80	2·80	55	16·2	20·2
4	11·4	0·80	2·80	31	28·8	35·8

(b) [Co phen$_3$]$^{2+}$–[Co phen$_2$]$^{2+}$ *exchange.* A solution for exchange was prepared by adding solid phenanthroline hydrate (516 mg.) to 0·198M-cobalt nitrate (5·0 c.c.), warming the whole to effect dissolution, and allowing the mixture to equilibrate at 0°. Such a solution contains approximately equal amounts of the tris- and the bis-species. [^{60}Co phen$_2$Cl$_2$],H$_2$O (6 mg.), well-powdered to facilitate dissolution, was added with vigorous shaking to initiate reaction. The exchange was stopped at various times by adding the solution to concentrated ammonium oxalate solution which immediately precipitated the bis-species as the ochre-yellow complex oxalate. This was rapidly centrifuged off and the clear supernatant liquid added to sodium perchlorate solution to precipitate the pale yellow perchlorate of the tris-complex. Both materials were washed with water, alcohol, and ether and radio-assayed. Thus the rates of fall in activity of the bis- and the increase in the tris-complex could be followed as the exchange [Co phen$_3$]$^{2+}$ + [^{60}Co phen$_2$]$^{2+}$ $\rightleftharpoons$ [Co phen$_2$]$^{2+}$ + [^{60}Co phen$_3$]$^{2+}$ proceeded. From the observations of a very small zero-time exchange for the tris-complex, the fall in activity of the bis-complex from the commencement to the completion of exchange (570 to 306 counts/min.) and the amounts of precipitates obtained from both exchange reactants, it was concluded that in these conditions about 54% of the phenanthroline-containing complex was in the bis-form and that separation was effective. The $t_{\frac{1}{2}}$ exchange values were 35 sec. (bis-end) and 42 sec. (tris-end), the latter being used as the more reliable result, so that

$$R_3 = k_3[\text{tris}] = \frac{0{\cdot}693}{t_{\frac{1}{2}}} \cdot \frac{[\text{bis}][\text{tris}]}{[\text{bis}] + [\text{tris}]}$$

and since [bis]([bis] + [tris]) = 306/570 (from the counts above), $k_3 = 8{\cdot}9 \times 10^{-3}$ sec.$^{-1}$ at 0·0°. A similar result was obtained in a second experiment.

(c) [Co phen]$^{2+}$–Co^{2+} *exchanges.* The mono-complex ion could be separated as an insoluble precipitate from cobalt(II) by adding either thiocyanate or disodium naphthalene-1 : 5-disulphonate. The latter was preferred because the precipitate of the complex salt was finer and could be easily " matted " on the aluminium planchettes. In all the runs, an excess (usually 5—10 times) of cobalt nitrate was added as a standard solution to phenanthroline hydrate and after warming to effect dissolution the exchange solution was equilibrated at the reaction temperature. Precautions to exclude oxygen were taken. ^{60}Cobalt nitrate solution was added and samples were removed at various times and plunged into an ice-cold solution of the precipitating agent. A pink precipitate of the complex was formed immediately and its appearance represented the exchange time. It was washed thrice with water, then alcohol and ether before being dried at 90° to the pentahydrate. It was radio-assayed in this form as a 14·0 ± 0·1 mg. mat on small planchettes. The efficiency of the separation was indicated by very small zero-time exchanges. Usually five separation points were taken to construct the normal exchange curve, which, in general, was an excellent first-order straight line. The results are shown in Table 2. Runs nos. 1—4 indicate that $R = k_1$[Co phen^{2+}] and is pH-independent between 4·6 and 5·8, both results expected in view of the more extensive investigation of the nickel analogue.[10] Since the cobalt complexes would be expected to have a lower stability than those of nickel, one run was performed with nearly 100-fold ratio of [Co^{2+}] to phenanthroline (no. 5) which ensures the formation of only the mono-species,[11] and although the rate was *decreased* this was shown to be almost completely as a result of the greatly increased ionic

[10] Wilkins and Williams, *J.*, 1957, 4514.
[11] Sone, Krumholz, and Stammreich, *J. Amer. Chem. Soc.*, 1955, **77**, 777.

XUM

strength (run no. 6). Finally runs 7—9 at different temperatures (with runs 1, 3, and 4) provided the data for a determination of the energy of activation as 19·4 ± 0·5 kcal. mole^{-1}.

(d) [Cu phen$_3$]$^{2+}$–phen *exchange*. There appears to be ample evidence both from spectral [12] and from potentiometric [13] data that in the presence of excess of phenanthroline, copper(II) ion forms the species [Cu phen$_3$]$^{2+}$. Copper chloride (0·08 mmole) and phenanthroline hydrate

TABLE 2. *Exchange of* [Co phen]$^{2+}$ *with* Co^{2+}.

Run no.	pH	Temp.	[Co phen^{2+}] (mmole l.$^{-1}$)	[Co^{2+}] (mmole l.$^{-1}$)	$t_{\frac{1}{2}}$ (sec.)	10^5R (sec.$^{-1}$ mole l.$^{-1}$)	10^3k (sec.$^{-1}$)
1	5·8	0·0°	15·2	135·6	540	1·75	1·15
2 [a]	4·6	0·0	15·3	143·2	570	1·68	1·09
3	5·3	0·0	15·3	253·6	590	1·69	1·11
4	5·5	0·0	30·6	238·8	500	3·76	1·23
5	5·5	0·0	15·2	1341·0	790	1·32	0·87
6 [b]	5·5	0·0	15·3	143·2	680	1·40	0·92
7	5·6	10·8	15·3	143·2	145	6·61	4·32
8	5·6	10·8	15·3	143·2	130	7·37	4·82
9	5·6	15·2	15·3	143·2	86	11·14	7·29

[a] Adjusted with HCl. [b] $NaNO_3$ added to adjust ionic strength to that of 5.

(0·5 mmole) were mixed in water (10 c.c.) and allowed to settle at 0°. An aqueous solution of [^{14}C]phenanthroline (3·6 mg. in 2 c.c.) at 0° was added. Addition of sodium perchlorate within 10 sec. precipitated [Cu phen$_3$]$(ClO_4)_2$[4] which showed equilibrium activity. This was checked in another run when the excess of ligand was extracted with chloroform and treated as in (a).

In exchanges (a) and (c), temperatures below that of the room were obtained by using an ordinary thermostat in a refrigerated room.

In all experiments (a)—(d) an end-window counter with ancillary electronic equipment was used for radioassay.

Acid Dissociation.—When the yellow [Co phen$_3$]$^{2+}$ ion is treated with acid, the colour diminishes rapidly as the ion dissociates to lower complexes. There are no distinct bands in the visible spectra of the tris-, bis-, or mono-species but the interpretation of the dissociation experiments is greatly assisted by the fact that between about 3700 and 4000 Å the molar extinction coefficient of the tris- is about three times that of the bis-complex, and almost ten times that of the mono-complex. At these wave-lengths, the absorption of phenH$^+$ and Co^{2+}, the other products of the dissociation, is negligible. In addition, the bis- and the mono-species dissociate more rapidly than the tris-species. Because of these facts, the time variation of the optical density of the complex solution is a direct measure of $-$d[tris]/dt, Beer's law having been shown to be obeyed for the tris-complex. An allowance is made for a small residual absorption at the end of the experiment by plotting $\log(d_t - d_\infty)/(d_0 - d_\infty)$ against time, where d_0, d_t, and d_∞ represent the optical density at the time of the first observation, at time t and at the conclusion of the experiment; straight lines were obtained over several half-lives and from these k_3 was calculated. The concentrations of [Co phen$_3$]$^{2+}$ used varied from 2 to 5 × 10^{-3}M, the acid used was 0·25—0·5M-hydrochloric acid, and the wave-lengths of observation were 3750 and 4000 Å (ε_M for the tris-species at these wave-lengths is 470 and 200 respectively). Despite the rapidity of the dissociation, after some practice surprisingly consistent results were obtained. Runs were carried out by using a Unicam S.P. 600 spectrophotometer at room temperature and at approx. 2°, in the latter case two of the four compartments of the cell holder being filled with ice and water. Temperatures were recorded for about 15 min. before, at the beginning of, and at the end of, the experiments which continued only for about 1 min. (room temperature) or 5 min. (2°). The spectra at the end indicated a large amount of mono-complex in the equilibrium mixture with these conditions. For three separate experiments at 16·5° ± 0·3°, $t_{\frac{1}{2}}$(diss) was determined as 11, 14, and 12 sec. from the 3750 Å observation, and 12 sec. from that at 4000 Å. From these a mean value for $k_3 = 5{\cdot}9 \times 10^{-2}$ sec.$^{-1}$ was calculated, compared with an exchange rate constant of $6{\cdot}7 \times 10^{-2}$ sec.$^{-1}$ estimated for that temperature. At 2·0° ± 0·5°, $t_{\frac{1}{2}}$(diss) = 78 sec., and $k_3 = 8{\cdot}9 \times 10^{-3}$ sec.$^{-1}$ ($k_{exch} = 10{\cdot}2 \times 10^{-3}$ sec.$^{-1}$). From these results an estimated energy of activation of 19·5 ± 1·0 kcal./mole was obtained. By adding fresh solutions of the complex [Co phen$_2$Cl$_2$],H$_2$O or solid [Co phenCl$_2$] to 0·5M-hydrochloric acid,

[12] Jørgensen, *Acta Chem. Scand.*, 1955, **9**, 1362.
[13] Pflaum and Brandt, *J. Amer. Chem. Soc.*, 1954, **76**, 6215.

$t_{\frac{1}{2}}$(diss) was observed to be <4 sec. and <2 sec. for the bis- and the mono-species respectively at 20°.

Discussion

The equilibria involved in this study can be represented as follows:

$$[\text{Co phen}_3]^{2+} \underset{}{\overset{R_3}{\rightleftharpoons}} [\text{Co phen}_2]^{2+} + \text{phen} \quad \ldots\ldots\ldots \quad k_3, k_{-3}$$

$$[\text{Co phen}_2]^{2+} \overset{R_2}{\rightleftharpoons} [\text{Co phen}]^{2+} + \text{phen} \quad \ldots\ldots\ldots \quad k_2, k_{-2}$$

$$[\text{Co phen}]^{2+} \overset{R_1}{\rightleftharpoons} \text{Co}^{2+} + \text{phen} \quad \ldots\ldots\ldots \quad k_1, k_{-1}$$

The exchange rate constant (k_{exch}) for the [Co $phen_3$]$^{2+}$–phen system can be directly equated to k_3, the dissociation rate constant for the tris-species. This follows since R_2 and R_1 will have relatively low values (bearing in mind the values of k_2 and k_1 from the acid dissociation work) with the conditions of ligand exchange.[10,14] In addition, the value for k_{exch} is similar to that of the [Co $phen_3$]$^{2+}$–[Co $phen_2$]$^{2+}$ exchange rate constant. From this study, $k_3 = 1{\cdot}4 \times 10^{16}$ exp $(-20{,}600/\boldsymbol{R}T)$ min.$^{-1}$. The similar value for k_3 in 0·5M-hydrochloric acid indicates that, as with the Fe(II) and Ni(II) analogues, dissociation is pH-independent in this range. The exchange results are not in conflict with those of West [5] who reported that the [Co $phen_3$]$^{2+}$–Co^{2+} exchange half-time was <28 sec. at 15°: his results are complicated however by the formation of chemical species, the mono- and bis-complexes, during the exchange process.

The rate of exchange of ^{60}Co between [Co phen]$^{2+}$ and Co^{2+} gives directly $k_1 = 1{\cdot}6 \times 10^{14}$ exp $(-19{,}400/\boldsymbol{R}T)$ min.$^{-1}$. It is apparent that, as for [Ni phen]$^{2+}$, the rate of dissociation is markedly pH-dependent.[10,15] Pfeiffer and Werdelmann [4] reported that [Co $phenCl_2$] develops a red colour with ferrous sulphate only after several minutes at room temperature (we have observed that half-formation of the final red colour requires at least 5 min. at 17°). Such a result appears at variance with our exchange data [$t_{\frac{1}{2}}$(exch) ~ 1 min. at 17°] until it is considered that there will be competition for released phenanthroline (see equilibrium R_1) between cobalt(II) and iron(II) and that the rate of formation of [Fe $phen_3$]$^{2+}$ will depend on the relative values of k_{-1} and the rate constant for the slowest step in the formation of ferroin.

Table 3. *Kinetic data and C.F.S.E. changes for the dissociation of* [M(phen)$_3$]$^{2+}$ *and* [M(phen)]$^{2+}$ *complexes.*

Electronic system	Complex ion	$\Delta S^{\ddagger}$ (e.u.)	E_{act} (kcal. mole^{-1})	ΔE (Dq) [16a]
d^3	V $phen_3^{2+}$	—	—	2
d^5	Mn $phen_3^{2+}$	—	—	0
d^6	Fe $phen_3^{2+}$ [a]	+28	32·1	4
d^7	Co $phen_3^{2+}$	+5	20·6	0
	Co $phen^{2+}$	−4	19·4	—
d^8	Ni $phen_3^{2+}$ [b]	+1	25·2	2
	Ni $phen^{2+}$ [c]	+5	26·2	—
d^9	Cu $phen_3^{2+}$		Fast	0
d^{10}	Zn $phen_3^{2+}$	—	—	0

[a] Basolo, Hayes, and Newmann, *J. Amer. Chem. Soc.*, 1954, **76**, 3807. [b] See ref. 9. [c] See ref. 10.

We shall now consider the entropies and energies of activation compared with analogous systems (see Table 3). The values for $\Delta S^{\ddagger}$ differ markedly from the high positive value for the [Fe $phen_3$]$^{2+}$ dissociation. The latter has been explained [16a] in terms of greater ligand freedom in an expanded state intermediate between diamagnetic [Fe $phen_3$]$^{2+}$ and the paramagnetic [Fe $phen_2$]$^{2+}$ dissociated fragment. Such a spin change does not occur

[14] Wilkins and Williams, *J. Inorg. Nuclear Chem.*, 1958, **6**, 52.
[15] Margerum, Bystroff, and Banks, *J. Amer. Chem. Soc.*, 1956, **78**, 4211.
[16] Basolo and Pearson, "Mechanisms of Inorganic Reactions," Wiley, New York, 1958, (*a*) p. 269, (*b*) p. 96 *et seq.*

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for the nickel(II) and cobalt(II) complexes and these have similar, more normal, values for $\Delta S^{\ddagger}$.

Basolo and Pearson have discussed,[16b] with particular reference to cobalt(III), the energies of activation which might be expected for different mechanisms (and transition states) for substitution. They proceed then to relate the rates of reactions of complex ions with the crystal field stabilisation energy (C.F.S.E.) for various *d*-electron systems and stereochemical configurations. We apply the reasoning developed by them to an understanding of the energies of activation of dissociation of Fe(II)–, Co(II)–, Ni(II)–, and Cu(II)–phenanthroline complexes. We assume that the dissociation of the complex involves a rate-determining "one-ended" detachment of one ligand and that for this process the transition state approximates to a combined square pyramid of nitrogen around the central metal plus two additional groups at a further distance, namely, one nitrogen of the leaving phenanthroline and one incoming water molecule. There will undoubtedly be some energy interaction with the entering water molecule and it would be impossible for us to calculate absolute energies of activation for such a scheme. However, it seems reasonable to suppose that, if this interaction with water and the other factors which influence the activation energy remains approximately constant for all these complexes which are extremely similar to one another in shape, etc., then the variations observed in the energy of activation from one complex to another will arise mainly from different changes in C.F.S.E. accompanying the octahedral to square-pyramid change (ΔE in Table 3), the latter approximating to the transition state for this purpose. A loss of C.F.S.E. would be expected to result in a slower reaction (higher energy of activation) than that of similar complex ion for which there was no loss of C.F.S.E. during the octahedral-square pyramid change. The C.F.S.E. change is indicated in Table 3 for the various ions, in terms of the Dq energy unit which from spectral data is about 3 kcal. mole^{-1} for bivalent transitional cations [17] and for [Ni phen$_3$]$^{2+}$ is 3·5 kcal. mole^{-1}.[12] A strong crystal field is assumed for the iron(II) case and a weak one for the manganese(II) and cobalt(II) complexes. It is considered that there is a retention of spin during the activation. An examination of Table 3 shows that the *differences* in activation energies for iron(II)–, cobalt(II)–, and nickel(II)–phenanthroline complexes do indeed fit very well with the ΔE values, and that it does appear that the other factors which influence the activation energy are similar for these complexes. A trigonal bipyramid or a pentagonal bipyramid as intermediate does not give the required relationship.[16b] Provided that the $\Delta S^{\ddagger}$ term is positive or only slightly negative, the exchanges of [Mn phen$_3$]$^{2+}$, [Cu phen$_3$]$^{2+}$, and [Zn phen$_3$]$^{2+}$ with [^{14}C]phenanthroline would be expected to be of the same order as with cobalt(II). Indeed, for the copper(II) case, $k \geqslant 0{\cdot}25$ sec.$^{-1}$ at 0° and this can be easily understood with an energy of activation only slightly less than 19 kcal. mole^{-1}. On the other hand, the positive value of ΔE for [V phen$_3$]$^{2+}$ indicates that, with this ion, slower rates might be expected, although its easy oxidation [18] might present experimental difficulties in any kinetic study.

Since optical forms of [Co phen$_3$]$^{2+}$ would be expected to racemise by a dissociative mechanism,[16a] much like [Ni phen$_3$]$^{2+}$, it may prove possible to resolve this ion despite its lability. The problem might be eased by using a ligand such as 4 : 7-dimethylphenanthroline since it is known that methyl ring-substitution in phenanthroline decreases the rate of dissociation of its metal complexes.[19]

The authors acknowledge very helpful correspondence with Professor Ralph G. Pearson regarding the subject matter of the discussion. They thank Imperial Chemical Industries Limited for the loan of a spectrophotometer and the University of Sheffield for an Alfred Tongue Scholarship (to P. E.).

THE UNIVERSITY, SHEFFIELD. [*Received, July* 23*rd*, 1958.]

[17] For a review of ligand-field theory see Griffith and Orgel, *Quart. Rev.*, 1957, **11**, 381.
[18] Brandt, Dwyer, and Gyarfas, *Chem. Rev.*, 1954, **54**, 959.
[19] Ellis and Wilkins, unpublished observations.

53. *Hydrolysis of Dialkylphosphinic Fluorides and Dialkyl Phosphorofluoridates. Kinetic and Tracer Studies.*

By M. HALMANN.

During hydrolysis in $H_2{}^{18}O$, no appreciable oxygen exchange occurs between water and the phosphoryl group of dimethylphosphinic fluoride, diethylphosphinic chloride, or di*iso*propyl phosphorofluoridate. A method for determining ^{18}O in $>PO{\cdot}OH$ groups is described. The uncatalysed hydrolysis of dimethylphosphinic fluoride is compared with that of some other acid halides. The deuterium isotope effect on the rate of the uncatalysed and of the acid-catalysed hydrolysis of di*iso*propyl phosphorofluoridate has been measured. Dimethylphosphinic fluoride has been synthesised from dimethylphosphinic chloride and sodium fluoride. Its hydrolysis is acid- and base-catalysed. The rate-determining step in the hydrolysis of these fluorides seems to involve both proton-transfer and nucleophilic attack.

THE solvolysis of phosphinic chlorides and phosphorochloridates has been shown to involve bimolecular nucleophilic displacement (S_N2) and not rapid reversible formation of unstable intermediates of quinquecovalent phosphorus.[1] Hydrolysis of these phosphorus chlorides is base-catalysed, but is unaffected by acids. In contrast, hydrolysis of dialkyl phosphorofluoridates is also acid-catalysed.[2,3] Similarly, the solvolysis of various alkyl and substituted benzyl fluorides is acid-catalysed, while there is no such catalysis in the reactions of the corresponding chlorides.[4]

Search for Intermediates: ^{18}O-*Exchange Studies.*—Oxygen-exchange during hydrolysis of various carbonyl compounds has been observed;[5] and exchange of oxygen in solutions of several inorganic phosphorus acids has been measured.[5] On the other hand, no oxygen-exchange was observed during the uncatalysed hydrolysis of phenyl phosphate.[6] Similarly, in the hydrolysis of several monoalkyl or aryl phosphates catalysed by prostatic acid phosphatase there was no evidence for reversible formation of an intermediate with five groups bonded to phosphorus.[7]

An expansion of the valency shell of phosphorus by interactions of *d*-orbitals and formation of unstable quinquecovalent intermediates is however *a priori* possible in reactions at phosphorus atoms. As an example of a stable quinquevalent compound of phosphorus, the successful preparation of pentaphenylphosphorus[8] may be cited.

The hydrolysis of di*iso*propyl phosphorofluoridate is subject to general acid- and base-catalysis.[3] Various mechanisms were proposed which all involved reversible addition of water to the phosphoryl group as a preliminary step.[3]

In the present work, evidence was sought for formation of intermediates during hydrolysis of phosphoryl compounds having substituents of different electronegative properties. No such evidence was found in the hydrolysis of diethyl phosphorochloridate.[1] A change in a direction which was thought to favour formation of intermediates was substitution of fluorine for chlorine. Fluorine is more electronegative than chlorine,[9] and the phosphorus–fluorine bond is stronger. It seemed therefore more likely that fast reversible addition of water to the phosphoryl group should be followed by a rate-determin-

[1] Dostrovsky and Halmann, *J.*, 1953, 502, 516; 1956, 1004.
[2] Waters and de Worms, *J.*, 1949, 926.
[3] Kilpatrick and Kilpatrick, *J. Phys. Colloid Chem.*, 1949, **53**, 1371, 1385.
[4] Miller and Bernstein, *J. Amer. Chem. Soc.*, 1948, **70**, 3600; Chapman and Levy, *J.*, 1952, 1673.
[5] Bender, Ginger, and Unik, *J. Amer. Chem. Soc.*, 1958, **80**, 1044, giving previous references; Brodskii and Sulima, *Doklady Akad. Nauk S.S.S.R.*, 1953, **92**, 589.
[6] Stein and Koshland, *Arch. Biochem. Biophys.*, 1952, **39**, 229.
[7] Bunton, Silver, and Vernon, *Proc. Chem. Soc.*, 1957, 348.
[8] Wittig and Riber, *Annalen*, 1949, **562**, 187.
[9] Pauling, "The Nature of the Chemical Bond," Cornell Univ. Press, Ithaca, New York, 1940, p. 60.

ing dissociation of fluorine than of chlorine from phosphorus. The hydrolysis of dimethylphosphinic fluoride and of di*iso*propyl phosphorofluoridate was carried out in ^{18}O-enriched water, and the phosphoryl group was analysed for ^{18}O content.

Dimethylphosphinyl fluoride was prepared by reaction of dimethylphosphinic chloride with sodium fluoride: $Me_2POCl + NaF = Me_2POF + NaCl$. The synthesis of several other dialkylphosphinic fluorides has recently been reported.[10]

Results for the hydrolysis of several phosphorus halides are given in Table 1. In experiments (*a*) and (*c*) the phosphorus halides were hydrolysed for more than ten half-times. The resulting dialkylphosphinic acid was analysed for ^{18}O-enrichment in the

TABLE 1. *Hydrolysis of phosphorus halides in* ^{18}O*-enriched water at* 25°.

Phosphorus halide	Water: Millimoles	Water: Atom % ^{18}O Excess	Reaction (%)	Atom % ^{18}O excess in PO·OH: Found	Atom % ^{18}O excess in PO·OH: Calc. for no exchange
(*a*) Me_2POF	1·40	16·5	100	0·60	0·59
(*b*) Me_2POF	1·30	556	50	0·02	0
(*c*) Et_2POCl	0·65	9·0	100	3·66	3·85
(*d*) $(Pr^iO)_2POF$ ...	0·406	278	30	0·02	0
(*e*) $(Pr^iO)_2POF$ ...	0·33	280 *	47	0·005	0

* Containing 0·093 millimole of HCl per l.

PO·OH group by the carbodi-imide method (see p. 309). In the other cases the unchanged phosphorus halide was extracted after partial hydrolysis, by chloroform for dimethylphosphinyl fluoride and by *n*-hexane for di*iso*propyl phosphorofluoridate.

In every case the observed value was close to that calculated for hydrolysis without exchange. Similar conclusions have been reached for the base-catalysed hydrolysis of phosphorus fluorides.[11]

Uncatalysed Hydrolysis of Phosphorus Fluorides.—For a discussion of the difference in reactivity of dialkyl phosphoro-chloridates and -fluoridates, the rate of the uncatalysed (" water ") reaction of the phosphorus fluorides will be compared with the rate of hydrolysis of similar chlorides.

The rate of hydrolysis of di*iso*propyl phosphorofluoridate in ordinary water has been measured by several methods.[2,3] The kinetics in ordinary water are complicated by autocatalysis by the product, di*iso*propyl hydrogen phosphate. At constant pH, the hydrolysis obeys first-order kinetics. Kilpatrick and Kilpatrick [3] measured the hydrolysis in buffer solution and determined the catalytic coefficients of the various components. By elimination of the parts of the reaction due to the catalysts, the rate constant of the water reaction, k_w, was found [3] to be 72×10^{-4} hr.$^{-1}$ at 25°. Waters and de Worms [2] measured the hydrolysis in ordinary water, and from the initial rate estimated k_w to be 60×10^{-4} hr.$^{-1}$ at 25°.

It seemed of interest to find a method of measuring the rate of the uncatalysed hydrolysis directly, by using a buffer system which contributes as little as possible to the reaction. The system fluoride ion–hydrofluoric acid, proposed by Bell and McCoubrey,[12] was very effective in decreasing the extent of the catalysed reactions in the hydrolysis of di*iso*propyl phosphorofluoridate. The relatively low dissociation constant of hydrofluoric acid [13] ($K_A = 6{\cdot}7 \times 10^{-4}$) ensures a low hydrogen-ion concentration, while the nucleophilic activity of the fluoride ion has no influence since the starting material is regenerated with the phosphorofluoridate.

In the present work, di*iso*propyl phosphorofluoridate was hydrolysed in aqueous sodium fluoride; the buffering action was sufficient to keep the concentration of hydrogen ions very low. The reaction followed first-order kinetics, which proved that the catalytic

[10] Dawson and Kennard, *J. Org. Chem.*, 1957, **22**, 1671.
[11] Larsson, *Acta Chem. Scand.*, 1957, **11**, 1139.
[12] Bell and McCoubrey, *Proc. Roy. Soc.*, 1956, **234**, *A*, 192.
[13] McCoubrey, *Trans. Faraday Soc.*, 1955, **51**, 743.

effect of undissociated hydrofluoric acid is negligible. At 25°, $k_1 = 62 \times 10^{-4}$ hr.$^{-1}$, in good agreement with published results.[2, 3]

The hydrolysis of dimethylphosphinic fluoride in ordinary water obeyed first-order kinetics, and the rate was similar to that measured in sodium fluoride solution. At 25°, $k_1 = (4 \pm 1) \times 10^{-4}$ sec.$^{-1}$. Its half-time is thus 1/230 that of di*iso*propyl phosphorofluoridate. The absence of autocatalysis in this case can be explained by the small dissociation constant of the product, dimethylphosphinic acid, the pK of which is about 3·1. The hydrogen-ion concentration from this acid and from hydrogen fluoride is insufficient to cause appreciable acid-catalysis. In 0·01N-hydrochloric acid, and in 0·05N-sodium hydroxide hydrolysis was complete within a few minutes.

In Table 2, the rates of hydrolysis of di*iso*propyl phosphorofluoridate at several temperatures are listed. From the temperature-dependence of the rate of hydrolysis, parameters of the Arrhenius equation were calculated: $k_1 = 0{\cdot}88 \times 10^{10} \exp(-21{,}800/RT)$ sec.$^{-1}$.

TABLE 2. *Hydrolysis of di*iso*propyl phosphorofluoridate in sodium fluoride solutions.*

Temp.	24·85°	24·85°	30·40°	30·40°	40·08°	40·08°
$POF(OPr^i)_2$ (millimole)	0·62	0·20	0·62	0·20	0·20	0·76
NaF (millimole)	24·5	24·5	24·5	24·5	24·5	6·1
10^3k_1 (hr.$^{-1}$)	6·2	6·2	12·4	11·8	37·8	36·4

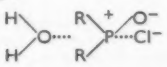
In the acid-catalysed hydrolysis of di*iso*propyl phosphorofluoridate, a much lower activation energy of 13·5 kcal. mole^{-1} has been observed.[3] Acid-catalysis is therefore due to reduction in the activation energy. The assumption [3] that the temperature coefficients of the uncatalysed and of the acid-catalysed hydrolysis are equal is thus untenable.

Comparison of Rates of Hydrolysis of Acid Fluorides and Chlorides.—In the previous section, the activation energy for the uncatalysed hydrolysis of di*iso*propyl phosphorofluoridate was reported as 21·8 kcal./mole. For the hydrolysis of di*iso*propyl phosphorochloridate, the much lower value of 14·4 has been reported.[1] Results for some other fluoro- and chloro-compounds are compared in Table 3. For the few compounds on which

TABLE 3. *Hydrolysis of fluorides and chlorides of phosphorus, sulphur, and carbon, at* 25°.

Acid halide	Solvent	10^4k_1 (sec.$^{-1}$)	ΔE^* (kcal. mole^{-1})	ΔS^* (cal. deg.$^{-1}$)	k_{RCl}/k_{RF}	Ref.
Me_2POF	H_2O	4	—	—	—	
Me_2POCl	EtOH (−8·5°)	60	—	—	—	1
$(Pr^iO)_2POF$	H_2O	0·017	21·8	−12·7	5000	
$(Pr^iO)_2POCl$	H_2O	81	14·4	−20·6		1
Ph·SO_2F	50% $COMe_2$	$<5 \times 10^{-4}$	—	—	<5000	14
Ph·SO_2Cl	,,	2·4	14	−29		14
Me·COF	75% $COMe_2$	1·1	—	—	8000	14
Me·COCl	,,	8600	14	−14		14
Ph_2CF	85% $COMe_2$	0·027	22·6	−10	1×10^6	14
Ph_2CCl	,,	27,000	12·5	−17		14

measurements at several temperatures have been made, the lower rate of hydrolysis of the fluoro-compound is due to a higher activation energy, and is in spite of a less negative entropy of activation. The ratio of the rates for chloro- and fluoro-compounds (Table 3) is similar for halides of phosphorus, sulphur, and carbon. The larger activation energy in fluoro-compounds seems to be connected with the larger bond energy of fluorine.[8] The more negative entropy of activation of acid chlorides seems due to the highly ordered, and possibly strained, transition state, *e.g.*,



The Deuterium Isotope Effect in Hydrolysis.—Comparison of the rates of solvolysis of various compounds in normal water and in deuterium oxide has sometimes been of use in

[14] Swain and Scott, *J. Amer. Chem. Soc.*, 1953, **75**, 246.

deciding between specific acid-catalysed reactions involving a fast reversible proton-addition followed by slow formation of the products, and proton-transfer in the rate-determining step.[15] The rate of hydrolysis of di*iso*propyl phosphorochloridate in deuterium oxide has been found [1] to be slightly smaller than that of water ($k_D/k_H = 0{\cdot}8$).

In the present work the rate of solvolysis of di*iso*propyl phosphorofluoridate was

TABLE 4. *Deuterium isotope effect in the solvolysis of diisopropyl phosphorofluoridate.*

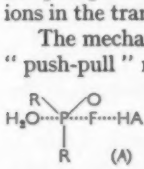
Temp.	$POF(OPr^i)_2$ (millimole) initially)	Solvent	Acid or buffer (millimole)	10^4k_1 (min.$^{-1}$)	k_D/k_H
24·85°	16·8	H_2O	HCl 48·8	32·5 ± 1·0	
,,	12·3	99·2% D_2O	DCl 52·0	32·4 ± 1·2	
,,	15·7	95% D_2O	DCl 46·4	27·8 ± 2·2	0·94 ± 0·03
,,	15·5	H_2O	HCl 20·7	16·7 ± 1·2	
,,	14·8	95% D_2O	DCl 22·5	17·6 ± 2·9	
40·08°	0·76	H_2O	NaF 6·09	6·3 ± 0·5	0·87 ± 0·06
,,	0·71	95% D_2O	NaF 4·53	5·5 ± 0·4	

measured in water and in deuterium oxide. The rates in water compared well with those reported by Waters and de Worms.[2] Table 4 lists first-order rate constants and their probable errors. The last two runs noted show the deuterium isotope effect in the uncatalysed hydrolysis in a sodium fluoride buffer.

In most acid-catalysed reactions the rate of solvolysis is larger in D_2O than in water. In these reactions a prior fast equilibrium between the acid and the substrate to form a protonated substrate is assumed to be followed by slow decomposition to the products. Most of the above reactions are subject to specific acid-catalysis, but even in many subject to general acid-catalysis a faster rate was found in deuterium oxide. A slower rate of hydrolysis in deuterium oxide than in water has been found in general acid-catalysed hydrolysis, involving a rate-determining proton-transfer.[16] In the hydrolysis of di*iso*propyl phosphorofluoridate, general acid-catalysis has been observed by kinetic measurements in buffer solutions.[3]

Discussion.—The lack of appreciable oxygen-exchange during the hydrolysis of phosphinic fluorides and phosphorofluoridates proves that addition of water to the phosphoryl group cannot be a preliminary fast and reversible step. The observations that hydrolysis is subject to general acid- and general base-catalysis and that it is slightly slower in deuterium oxide seem to indicate that proton-transfer occurs as part of the rate-determining step. The much higher activation energy of di*iso*propyl phosphorofluoridate than of the phosphorochloridate shows that breakage of the phosphorus–fluorine bond must also be part of the rate-determining step. The less negative entropy of activation of the phosphorofluoridate may be due to unfreezing of water molecules from the hydrogen ions in the transition state.

The mechanism which seems best to describe the experimental results is a termolecular " push-pull " mechanism,[17] with the general acid catalyst HA as the electrophilic reagent, and water or some other base as the nucleophilic reagent. The transition state may then be visualised as (*A*). Other electrophilic reagents, such as chelated Cu(II) may act [18] instead of the acid HA. Alternatively, a two-step mechanism may be proposed for acid-catalysis with rate-determining proton-transfer in the first step, followed by fast addition of water to the phosphorus atom. Such a mechanism does not, however, account for the base-catalysis observed, and for the slight effect of ionic strength.



(*A*)

[15] Reitz, *Z. phys. Chem.*, 1937, *A*, **179**, 119; Bell, " Acid–Base Catalysis," Oxford Univ. Press, 1941, pp. 143—152; Leffler and Grunwald in " Technique of Organic Chemistry," Interscience Publ., New York, 1953, Vol. VIII, pp. 319—322; Wiberg, *Chem. Rev.*, 1955, **55**, 713; Pritchard and Long, *J. Amer. Chem. Soc.*, 1956, **78**, 6009; Challis, Long, and Pocker, *J.*, 1957, 4679.

[16] Long, Congress Handbook, XVIth Congress Internat. Union Pure Appl. Chem., p. 28, Paris, July 1957; Long and Watson, *J.*, 1958, 2022.

[17] Swain, *J. Amer. Chem. Soc.*, 1950, **72**, 4578.

[18] Courtney, Gustafson, Westerback, Hyytiainen, Chaberek, and Martell, *ibid.*, 1957, **79**, 3030.

Experimental

Materials.—Dimethylphosphinic chloride [19] (3·85 g.), carbon tetrachloride (15 ml.), and sodium fluoride (4·2 g.) were refluxed for 2½ hr. The product was distilled at atmospheric pressure, yielding 1·8 g. (55%) of *dimethylphosphinic fluoride*, b. p. 169—171° (Found: F, 19·2. C_2H_6OFP requires F, 19·8%). The colourless liquid is easily soluble in benzene, chloroform, and *p*-xylene, fairly soluble in water, and only slightly soluble in *n*-hexane.

Di*iso*propyl phosphorofluoridate was obtained by Saunders and Stacey's method.[19a]

Diethylphosphinic acid was obtained either by reaction of ethylmagnesium bromide with thiophosphoryl chloride,[19] or by addition of bromine to chlorodiethylphosphine, followed by hydrolysis of the resulting phosphonium chloride: $Et_2PCl + Br_2 = Et_2PClBr_2$; $Et_2PClBr_2 + 2H_2O = Et_2PO{\cdot}OH + 2HBr + HCl$. To chlorodiethylphosphine [20] (1·45 g.), a 0·4N-solution of bromine in carbon tetrachloride (50 ml.) was added slowly. A white precipitate was formed. Water was added in excess and the mixture was evaporated on the steam-bath. The residual oil was dried at 100° under reduced pressure. To the diethylphosphinic acid formed, benzene (10 ml.) and phosphorus pentachloride (2·4 g.) were added and the mixture was refluxed for 1 hr., then distilled twice under reduced pressure (b. p. 95°/8 mm.), yielding 0·5 g. (31%) of a colourless liquid (Found: Cl, 25·7. Calc. for $C_4H_{10}OClP$: Cl, 25·3%).

^{18}O-Enriched water was obtained from the fractionating plant of this Institute. Its ^{18}O-content was determined by distilling about 0·04 mole of normal carbon dioxide into an evacuated break-seal tube [21] containing about 0·1 g. of water. The tube was sealed and after storage overnight at 70° for equilibration, the ratio of masses 46 : 44 was determined by a Consolidated Engineering Corporation Model 21-401 mass spectrometer. The atom % concentration of ^{18}O in the water was calculated from this ratio.[22]

Analysis of ^{18}O in PO·OH Groups.—Di-*p*-tolylcarbodi-imide (0·1 g.; L. Light & Co.) in dry *n*-hexane or ether (4 ml.) was freed from insoluble material by centrifugation. A solution of dialkylphosphinic acid or dialkyl hydrogen phosphate in dry dioxan or ether (5 ml.) was added. Di-*p*-tolylurea crystallised: [23] $2R_2PO{\cdot}OH + ArN{:}C{:}NAr \longrightarrow (R_2PO)_2O + (Ar{\cdot}NH)_2CO$. Next morning the crystals were centrifuged off, washed several times with dry ether and once with *n*-hexane, and dried under reduced pressure; they had m. p. 277° (reported [24] for di-*p*-tolylurea, m. p. 260°). An attempt was made to base the ^{18}O-determination on the observation that [25] di-*p*-tolylurea at 300° decomposes to carbon dioxide, *p*-toluidine, and *NN'N''*-tri-*p*-tolylguanidine: however, pure di-*p*-tolylurea in evacuated bulbs did not produce carbon dioxide at this temperature. In the presence of small amounts of copper bronze (Triple deep gold bronze powder, Magna Manuf. Co., Inc., N.Y., dried in a hydrogen stream at 300 to 400° for 1 hr.), quantitative decomposition of di-*p*-tolylurea occurred, and the products described by Barr were isolated. Samples of di-*p*-tolylurea (about 30 mg.) with copper bronze (about 1 mg.) were sealed under vacuum in a break-seal tube [20] and heated to 320° for 0·5 hr. The carbon dioxide formed was analysed mass-spectrometrically.

Hydrolysis of Dimethylphosphinic Fluoride in ^{18}O-Enriched Water.—(a) *Complete reaction.* Dimethylphosphinic fluoride (0·135 g.) and enriched water (0·297 g.; 1·17 atom % excess ^{18}O) were mixed and kept in a thermostat at 25° for 2 hr. The water was then evaporated in a vacuum, and the remaining white crystals of dimethylphosphinic acid were suspended in dry dioxan (1 ml.) and were added to a solution of di-*p*-tolylcarbodi-imide for ^{18}O-analysis.

(b) *Partial reaction.* Dimethylphosphinic fluoride (0·125 g.) was dissolved in enriched water (10 ml.; 1·17 atom % excess ^{18}O); after 4 min. chloroform (10 ml.) was added. The mixture was shaken and the layers were separated. The distribution coefficient of dimethylphosphinic acid between water and chloroform had separately been determined as 73 : 1. The chloroform layer was evaporated under reduced pressure and the residue of dimethylphosphinic fluoride was hydrolysed by addition of 1 ml. of normal water. After several hours the water was distilled off in a vacuum-system. The remaining dry dimethylphosphinic acid was dissolved in 1 ml. of

[19] Kabachnik and Shepeleva, *Izvest. Akad. Nauk S.S.S.R., Otdel. khim. Nauk*, 1949, **1**, 56; Kosolapoff and Watson, *J. Amer. Chem. Soc.*, 1951, **73**, 5466.
[19a] Saunders and Stacey, *J.*, 1948, 698.
[20] Beeby and Mann, *J.*, 1951, 413.
[21] Rittenberg and Ponticorvo, *Internat. J. Appl. Rad. Isot.*, 1956, **1**, 208.
[22] Dostrovsky and Klein, *Analyt. Chem.*, 1952, **24**, 414.
[23] Khorana and Todd, *J.*, 1953, 2259; Khorana, *Chem. Rev.*, 1953, **53**, 145.
[24] Manuelli and Ricca-Rosellini, *Gazzetta*, 1899, **29**, II, 124.
[25] Barr, *Ber.*, 1886, **19**, 1768.

dry benzene by gentle warming and was added to a solution of di-*p*-tolylcarbodi-imide in *n*-hexane. Carbon dioxide obtained from the precipitated di-*p*-tolylurea contained 0·01 atom % excess ^{18}O. In the dimethylphosphinic fluoride in the chloroform layer, before its hydrolysis in normal water the content of ^{18}O in the phosphoryl group must have been not more than 0·02 atom % excess.

Hydrolysis of diethylphosphinic chloride was carried out as described in (a). Hydrolysis of di*iso*propyl phosphorofluoridate was carried out as described in (b), except that *n*-hexane was used as extractant.

Kinetics of Hydrolysis.—The required solutions of the phosphorus fluorides were prepared in volumetric flasks and kept in polyethylene bottles in a thermostat bath. Aliquot parts were withdrawn and analysed for fluoride ions (thorium nitrate and sodium alizarinsulphonate) or for unchanged phosphorus fluoride (hydrogen peroxide and *o*-dianisidine hydrochloride [26]). Two examples are tabulated.

Hydrolysis of dimethylphosphinyl fluoride (initially 0·008 *molar) in water at* 24·85°.

Time (sec.)	0	307	560	1088	1500	2294	∞
0·00911N-$Th(NO_3)_4$ (ml.) ...	1·55	2·23	2·48	2·79	3·00	3·60	4·45

From the slope of a plot of log $(a - x)$ against time, the first-order rate-constant (k_1) was calculated to be $4·0 \times 10^{-4}$ sec.$^{-1}$.

*Hydrolysis of di*iso*propyl phosphorofluoridate (initially* 0·196 *millimolar) in* 0·0246M-*sodium fluoride at* 24·85°. o-*Dianisidine method.*

Time (hr.)	0	25·5	48	72·3	141·3	164·5	240	313
Optical density ...	0·383	0·290	0·263	0·240	0·141	0·110	0·0775	0·0555

From the slope of a plot of log (opt. dens.) against time, the first-order rate-constant (k_1) was calculated to be 0·00624 hr.$^{-1}$.

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[26] Marsh and Neale, *Chem. and Ind.*, 1956, 494.

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54. *Reactions of Tin*(IV) *Halides with Ammonia Derivatives. Part III.*[1] *The Reaction of Tin*(IV) *Halides with Aliphatic Amines.*

By E. BANNISTER and G. W. A. FOWLES.

The reactions of tin(IV) chloride, tin(IV) bromide, and tin(IV) iodide with trimethylamine, dimethylamine, methylamine, and a number of higher primary amines have been investigated. Whereas simple 1 : 2 adducts are formed by all three halides with trimethylamine, and by tin(IV) chloride with dimethylamine, tin(IV) bromide and tin(IV) iodide react further with dimethylamine. The halides react with methylamine to give as final product a mixture of methylamine hydrohalide and the appropriate aminobasic tin(IV) halide, $SnX_2(NHMe)_2,2NH_2Me$.

The mechanism of the reactions and the structure of the products are discussed, and a number of anomalies in the literature are re-interpreted.

REACTIONS of tin(IV) halides with ammonia have recently been studied [1,2] in some detail; the chloride, bromide, and iodide form simple diammoniates ($SnX_4,2NH_3$) in gas-phase reactions, but are ammonolysed in liquid ammonia. The reactions of the tin(IV) halides with tertiary amines and several other nitrogen compounds have been examined by a number of workers, who obtained adducts of formula $SnX_4,2A$ in most cases, for instance

[1] Part II, Bannister and Fowles, *J.*, 1958, 4374.
[2] Bannister and Fowles, *J.*, 1958, 751.

in reactions of tin(IV) chloride with trimethylamine,[3] triethylamine,[4] pyridine,[3,5] pyrrole and substituted pyrroles,[6] indole,[7] and several nitriles,[8] of tin(IV) bromide with trimethylamine,[9] triethylamine,[9] and substituted pyrroles,[6] and of tin(IV) iodide with pyridine [10] and aniline.[11] Corresponding tertiary phosphine and arsine compounds have also been reported.[12] In these simple adducts, the tin(IV) halide acts as a typical Lewis acid by accepting electrons from the nitrogen atoms of the ligands; in this way the tin atom achieves an octahedral configuration ($5s5p^35d^2$). In presence of the amine hydrohalide, the hexahalogenostannate(IV) complex may be formed,[13,14] *e.g.*, $[PhNH_3]_2[SnBr_6]$.

Both tin(IV) chloride [4] and tin(IV) bromide [9] form tetra-aminates with triethylamine, so it appears that the tin atom might attain a covalency of eight under suitable conditions; this point is deal with in the Discussion.

Much less is known of the reactions of the tin(IV) halides with secondary and primary aliphatic amines. George, Mark, and Wechster [15] obtained diaminates from the reaction of tin(IV) chloride with *sec.*-butylamine and *n*-butylamine, and Trost [16] obtained a hexaaminate with ethylamine and tin(IV) chloride. Although the diaminates can be considered simple adducts, the tin atom is unable to achieve a covalency of ten, so that the ethylamine product cannot be just an addition compound. With the primary and secondary amines, the presence of a nitrogen–hydrogen bond makes aminolysis of the tin(IV) halides probable, so that the ethylamine compound might be considered a mixture of ethylamine hydrochloride and an aminobasic tin(IV) chloride.

Since Trost's work is the only indication of the aminolysis of tin(IV) halides and the formation of covalent tin–nitrogen bonds, we have examined the reactions of the three tin(IV) halides with a number of aliphatic primary amines, and with dimethylamine. The reaction of trimethylamine with tin(IV) bromide and tin(IV) iodide has also been studied to make sure that only simple diaminates are formed. (The work of Bohme and Boll [9] on the tin(IV) bromide–trimethylamine system was published during our investigations).

Experimental

Materials.—Tin (IV) halides,[1,2] mono-, di-, and trimethylamine,[17] and ethylenediamine [18] were purified as described previously. *n*-Propylamine, *n*-butylamine, and *n*-pentylamine (Messrs. British Drug Houses) were all dried by distillation *in vacuo* from freshly-crushed barium oxide.

Analyses.—Tin, halogen, and nitrogen were estimated as usual,[1,2] on weighed samples whenever possible, but where the product adhered very firmly to the sides of the reaction vessel, it was hydrolysed *in situ*; in such cases ratios only are quoted.

Reactions.—The appropriate tin(IV) halide and amine were allowed to react in the absence of solvents in the usual type of closed vacuum system.[17] Initial experiments were carried out in a detachable jointed tube complete with stopcock, by condensing excess of amine on a weighed quantity of tin(IV) halide; after reaction for an hour or so (with shaking) at room temperature, excess of amine was pumped off and the tube reweighed. The amount of amine associated with the halide could therefore be determined.

To find out if further reaction would take place on standing, the tin(IV) halide and excess of

[3] Laubengayer and Smith, *J. Amer. Chem. Soc.*, 1954, **76**, 5985.
[4] Trost, *Canad. J. Chem.*, 1952, **30**, 835.
[5] Pfeiffer, *Z. anorg. Chem.*, 1910, **71**, 97.
[6] Schmitz-Dumont, *Ber.*, 1929, **62**, *B*, 226.
[7] Schmitz-Dumont and Motzkus, *Ber.*, 1929, **62**, *B*, 466.
[8] Ulich, Hertel, and Nespital, *Z. phys. Chem.*, 1932, *B*, **17**, 21.
[9] Böhme and Boll, *Z. anorg. Chem.*, 1957, **292**, 61.
[10] Dimitriou, *Praktika*, 1927, **2**, 496.
[11] Cooper and Wardlaw, *J.*, 1930, 1141.
[12] Allison and Mann, *J.*, 1949, 2915.
[13] Rosenheim and Aron, *Z. anorg. Chem.*, 1904, **39**, 170.
[14] Richardson and Adams, *Amer. Chem. J.*, 1899, **22**, 446.
[15] George, Mark, and Wechster, *J. Amer. Chem. Soc.*, 1950, **72**, 3896.
[16] Trost, *Canad. J. Chem.*, 1952, **30**, 842.
[17] Fowles and Pleass, *J.*, 1957, 1674.
[18] Fowles, McGregor, and Symons, *J.*, 1957, 3329.

amine were sealed in ampoules and allowed to react (after 24 hours' mechanical shaking) for several months. The ampoules were then opened and the contents analysed after excess of amine had been pumped off. In some instances, the products were extracted with solvents before analysis, but unless this is stated the analytical figures refer to the total solid remaining after removal of amine. All experiments were carried out two or three times.

(i) *Reaction of trimethylamine with tin*(IV) *bromide and tin*(IV) *iodide.* The pale yellow solid initially formed by tin(IV) bromide had an overall composition $SnBr_4,2{\cdot}0NMe_3$. After reaction with trimethylamine for several months in sealed ampoules, both tin(IV) bromide and tin(IV) iodide formed *diaminates* [Found: (*a*) Sn, 21·4; Br, 57·9; N, 5·05. $SnBr_4,2NMe_3$ requires Sn, 21·3; Br, 57·4; N, 5·03%. (*b*) Sn : I : N = 1·00 : 4·00 : 2·00]. The pale yellow diaminate of tin(IV) bromide was insoluble in trimethylamine, but the brown compound formed by tin(IV) iodide was fairly soluble and gave an amber solution in the amine.

(ii) *Reaction of dimethylamine with tin*(IV) *halides.* In initial experiments, tin(IV) chloride and tin(IV) iodide both reacted with dimethylamine to give adducts $SnCl_4,1{\cdot}95NHMe_2$ and $SnI_4,2{\cdot}21NHMe_2$. The reaction of tin(IV) bromide and dimethylamine was very rapid and could not be examined by the weighed-vessel technique since the sudden pressure change invariably burst the vessel. The *diaminate* formed by tin(IV) chloride sublimed unchanged on heating *in vacuo* to 156° (Found : Sn, 34·1 ; Cl, 40·8; N, 7·92. $SnCl_4,2NHMe_2$ requires Sn, 33·9 ; Cl, 40·4 ; N, 7·90%). In nitrogen, the sublimate melted to a brown liquid at 197°.

On reaction for several months in an ampoule, tin (IV) chloride still only formed the white diaminate, since the product again melted at 197° (Found: Cl, 39·8; N, 7·92%). With tin(IV) bromide, however, a pale yellow solid remained on removal of amine from the amber solution (Found: Sn, 21·5; Br, 57·8; N, 6·87%, *i.e.*, Sn : Br : N = 1·00 : 3·99 : 2·70). The yellow solution formed by tin(IV) iodide in dimethylamine deposited a white solid on cooling to −78°, but removal of amine left a heterogeneous brown solid $SnI_4,3{\cdot}8NHMe_2$; another similar product which was pumped for 4 hr. at 50° before analysis, gave Sn, 15·1; I, 64·3; N, 6·43%, *i.e.*, Sn : I : N = 1·00 : 3·98 : 3·61.

(iii) *Reaction of monomethylamine with tin*(IV) *halides.* In initial reactions, both tin(IV) chloride and tin(IV) bromide gave white products $SnX_4,4{\cdot}0NH_2Me$. When heated to 200° *in vacuo*, the tin(IV) chloride product turned yellow, evolved methylamine, and gave a substantial white sublimate; on prolonged heating virtually all the solid sublimed (Found: Sn : Cl : N = 1·00 : 3·96 : 2·01).

When sealed in ampoules, all three tin(IV) halides dissolved in the methylamine to give colourless solutions, which after some hours became cloudy and slowly formed a white deposit. This redissolved on warming. The white products obtained after reaction for several months had somewhat similar compositions (Found: Sn : Cl : N, 1·00 : 3·99 : 5·69; Sn : Br : N, 1·00 : 4·06 : 5·83; Sn : I : N, 1·00 : 4·00 : 5·60). When the iodide product was pumped at 50° for 2 hr. before analysis, the product was $SnI_4,5{\cdot}4NH_2Me$. It seemed likely that all those products were mixtures of aminobasic tin(IV) halides and the appropriate methylamine hydrohalide, and attempts were accordingly made to obtain pure substances by selective solvent extraction. Although nothing could be extracted from the tin(IV) chloride product by benzene, chlorobenzene, or chloroform, a small amount of solid was obtained by several extractions with nitromethane. Since this solid contained no tin (Found: N : Cl = 1·08 : 1·00), it was probably methylamine hydrochloride. However, its low solubility in nitromethane prevented its complete removal from the products and the isolation of a pure aminobasic tin(IV) chloride. The methylamine hydrohalides readily dissolved in methylamine, but in the case of the tin(IV) chloride and tin(IV) iodide products the tin-containing component of the mixture was too soluble for effective separation. With the tin(IV) bromide product, however, an appreciable amount of white solid still remained after several washings with 50 ml. of methylamine. After removal of excess of amine, the insoluble and soluble portions were hydrolysed *in situ* and analysed (Found: Sn : Br : N, 1·00 : 2·10 : 4·14, for insoluble; Sn : Br : N, 1·00 : 16·7 : 18·6, for soluble). Apparently the methylamine largely extracts methylamine hydrobromide, leaving a relatively insoluble aminobasic tin(IV) bromide, $SnBr_2(NHMe)_2,2NH_2Me$. Some of this tin compound is also found as expected in the soluble portion, where the overall analysis suggests a mixture of $SnBr_2(NHMe)_2,2NH_2Me$ + 14·6 mol. of NH_2Me,HBr.

(iv) *Reaction of tin*(IV) *iodide with ethylenediamine and higher primary aliphatic amines.* Tin(IV) iodide dissolved in *n*-propylamine, *n*-butylamine, and *n*-pentylamine to give yellow

solutions which did not change appreciably on standing for some months. When excess of amine was pumped away, the solutions became viscous yellow glasses from which the amine could only be removed very slowly even at 45°. The overall compositions of the products are tabulated.

Products of the reaction of tin(IV) *iodide with aliphatic amines.*

Amine	Product (A = amine)	Reaction time	Pumping before analysis
n-Propylamine ...	SnI_4,4·21A	Few hours	20 hr. at 45°
	SnI_4,4·71A	Several months	24 hr. at 45°
n-Butylamine	SnI_4,6·37A	Few hours	4 hr. at room temp.
	SnI_4,4·94A	Few hours	4 hr. at room temp. and 1 hr. at 45°
	SnI_4,4·80A	Several months	24 hr. at 45°
n-Pentylamine	SnI_4,8·8A	Several months	24 hr. at room temp.

Tin(IV) iodide reacted with ethylenediamine to give a white solid and a colourless solution. The solid was filtered off and washed with ethylenediamine (5 × 50 ml.) to remove any ethylenediamine hydriodide and pumped (Found: Sn : I : N, 1·00 : 0·96 : 3·62). A glass remained when excess of ethylenediamine was removed from the extract; this is characteristic of concentrated solutions in ethylenediamine.[19]

Discussion

All three tin(IV) halides give the simple 1 : 2 adducts with trimethylamine, and even after several months' reaction there was no evidence for the formation of higher aminates. It is, therefore, surprising that a tetra-aminate is formed by triethylamine, because although triethylamine is a stronger base, its steric requirements are much greater, and its complexes are accordingly less stable.[20,21] Probably the tin atom is not octaco-ordinated as suggested by Trost,[4] who pointed out, however, that the tetra-aminate is unlikely to be a mixture such as $SnX_2(NEt_2)_2 + 2NEt_4Cl$; the sharp m. p. (90—92° [9]) supports this supposition. Böhme and Bolle suggested an ionic structure, $[Sn(NEt_3)_4]^{4+}4Br^-$, since the tetra-aminate has a completely different nature from the diaminate, for instance, in being soluble in water. They argue that since all the bromine is precipitated by silver nitrate, then it is entirely ionic. The bromine atoms would be labile in any structure, however, so that there is no evidence for the ionisation of all the tin–bromine bonds; this would, indeed, be unlikely as the preparation was made in an organic solvent. The properties are consistent with some measure of ionisation, however, and a structure $[SnBr_2(NEt_3)_4]^{2+}2Br^-$ is perhaps more likely, since it gives an octahedral configuration to the tin atom.

From an aqueous solution of the tetra-aminate, Böhme and Boll isolated $[Sn(NEt_3)_6]^{4+}4NO_3^-$. Complete ionisation is reasonable with a preparation made in aqueous solution, but since this product contains hexaco-ordinated tin it is reasonable to suppose the original tetra-aminate does also. We consider that both trimethylamine and triethylamine form simple diaminates, but that the more basic triethylamine can also force some ionisation of the tin–bromine bonds.

The reaction of dimethylamine with tin(IV) chloride again gives only a 1 : 2 adduct which sublimes unchanged *in vacuo*. The 1 : 2 di-*n*-butylamine compound reported by George *et al.*[15] is evidently similar. With tin(IV) bromide and tin(IV) iodide, however, more dimethylamine is taken up on prolonged reaction, and the final products have compositions $SnBr_4$,2·7$NHMe_2$ and SnI_4,3·8$NHMe_2$ respectively. In view of their non-stoicheiometric compositions and heterogeneous appearance, it seems reasonable to consider these products to be mixtures of di- and tetra-aminates. The nature of the tetra-aminate is again difficult to formulate, since although the dimethylamine molecule forms stronger

[19] Fowles and McGregor, *J.*, 1958, 136.
[20] Brown, Schlesinger, and Cardon, *J. Amer. Chem. Soc.*, 1942, **64**, 325.
[21] Brown and Sujishi, *J. Amer. Chem. Soc.*, 1948, **70**, 2878.

complexes [22] than does trimethylamine, it is still doubtful whether the tin(IV) halide can accept four dimethylamine molecules and give the tin atom an octaco-ordinated configuration. In any case, tin(IV) chloride should be a better Lewis acid than tin(IV) iodide, and yet it shows no tendency to accept more than two molecules of dimethylamine. Moreover, it seems odd that only part of the tin(IV) bromide should form a tetra-aminate when the amine is present in such huge excess.

The two most likely structural possibilities are then either an ionic complex similar to that suggested for $SnX_4,4NEt_3$, *e.g.*, $[SnX_2(NHMe_2)_4]^{2+}2X^-$ or a mixture of aminolysis products, *e.g.*, $SnX_3(NMe_2),2NHMe_2 + NHMe_2,HX$. Whereas the ionic formulation was considered correct for the triethylamine adduct, aminolysis is more likely with dimethylamine since a nitrogen–hydrogen bond is broken more readily than a nitrogen–carbon bond; this type of reaction has in fact been firmly established for several metal halide–dimethylamine reactions.[17,23] Moreover, in the case of the tin(IV) iodide product, the composition $SnI_4,3{\cdot}8NHMe_2$ indicates almost quantitative formation of the tetra-aminate, and yet the very heterogeneous nature of the product shows that it must be a mixture and not a single species as required by the ionic structure. It is also more feasible to consider the tin(IV) bromide product as resulting from an incomplete aminolysis rather than an incomplete ionisation.

With monomethylamine, the tin(IV) halides initially form a tetra-aminate, but further reaction takes place after some hours, and a white precipitate begins to form; the eventual composition of the reaction product approximates to $SnX_4,6NH_2Me$. While it seems fairly obvious that the second slow reaction is aminolytic, there are three possible explanations of the overall reaction:

(i) $SnX_4 + 4NH_2Me = SnX_4,4NH_2Me \xrightarrow{+2NH_2Me} SnX_3(NHMe),4NH_2Me + NH_2Me,HX$

(ii) $SnX_4 + 4NH_2Me = SnX_4,4NH_2Me \xrightarrow{+2NH_2Me} SnX_2(NHMe)_2,2NH_2Me + 2NH_2Me,HX$

(iii) $SnX_4 + 4NH_2Me = SnX_3(NHMe),2NH_2Me + NH_2Me,HX \xrightarrow{+2NH_2Me} SnX_2(NHMe)_2,2NH_2Me + 2NH_2Me,HX$

Isolation of the aminobasic tin(IV) bromide $SnBr_2(NHMe)_2,2NH_2Me$ from the tin(IV) bromide product shows that reaction (i) is incorrect. It is difficult to choose between the other two possibilities, since it really amounts to deciding whether the tetra-aminate is a simple adduct or a mixture. Although the adduct requires the tin atom to be octaco-ordinated, this is not perhaps so unreasonable with monomethylamine as the ligand. Moreover, the tetra-aminate formed by tin(IV) chloride loses methylamine when heated *in vacuo* and forms the di-aminate as a sublimate almost quantitatively. This di-aminate could, however, result from the reaction $SnCl_3(NHMe) + NH_2Me,HCl = SnCl_4,2NH_2Me$. It is noteworthy that although the di-adducts of tin(IV) chloride with ammonia, methylamine, and dimethylamine are volatile, Laubengayer and Smith were unable to purify the analogous trimethylamine adduct by sublimation. That the composition of products of the prolonged reactions should fall rather below $SnX_4,6NH_2Me$ is not unexpected, because two molecules of amine are attached to an aminobasic tin(IV) halide, and these replaced compounds will be much poorer Lewis acids than the halides themselves, and will tend to lose amine on pumping.

Trost observed that tin(IV) chloride added 6 mol. of ethylamine, 1·4 mol. of which were lost on heating *in vacuo* at 88°. It seems reasonable to suppose that Trost's product is also a mixture, $SnCl_2(NHEt)_2,2NH_2Et + 2NH_2Et,HCl$, and that the two co-ordinately-bound ethylamine molecules will be lost on heating *in vacuo*. Although Trost only obtained 1·4 mol. of ethylamine, he did not apparently heat the product above 88°, and it is likely that the amine was incompletely removed under these conditions, since it would diffuse only slowly through the solid lattice.

[22] Brown and Taylor, *J. Amer. Chem. Soc.*, 1947, **69**, 1332.
[23] Fowles and Pleass, *J.*, 1957, 2078.

n-Butylamine only gave a di-aminate according to George and his co-workers. Their compound being assumed to have the stated composition (the only analysis is for nitrogen), then it is apparent that solvolysis decreases as the alkyl group gets larger. Although the extension of our work to *n*-propylamine, *n*-butylamine, and *n*-pentylamine yielded only glasses from which free amine could be only incompletely removed, our figures show that much less reaction has occurred than with methylamine and ethylamine, so that the nature of the alkyl group does determine the reaction.

In the reaction of tin(IV) iodide with ethylenediamine, three of the tin–iodine bonds are aminolysed, and this we attribute to the highly basic nature of the ethylenediamine and to the possibility of chelate formation.

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55. *Acetyl Chloride as a Polar Solvent. Part I. Solubility of Substances and Formation of Solvates in Acetyl Chloride.*

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Solubilities of substances, including Lewis acids and bases, and formation of solvates in acetyl chloride have been studied. Conductivities of the solutions of Lewis acids and bases indicate formation of ion pairs. The constitution of these solutions is discussed.

THE high dipole moment,[1] comparatively long and weak carbon–chlorine bond,[2,3] and high reactivity (in which respect it resembles nitrosyl chloride[4]) suggest that acetyl chloride ionizes into acetylium and chloride ions, just as nitrosyl chloride ionizes into nitrosyl and chloride ions.[5] The relatively high dielectric constant of acetyl chloride (15·9 at 20°; cf. carbonyl chloride 4·32 at 22°[7]) and its convenient working range (m. p. −112°, b. p. 51·8°) should render it a fairly good solvent.

The solubilities (*S*, in g./100 g. of solvent) of a number of chlorides at 30° ± 0·1° are recorded in Table 1(a). In some cases, the solubility was determined only qualitatively to explore the possibility of the formation of solvates. These results are given in Table 1(b).

Strongly ionic chlorides were insoluble in acetyl chloride, as were such other salts as silver and potassium nitrate, copper and cadmium carbonate, and sodium nitrite. During the determination of the solubility of oxides, it has been found that the mixtures with acetyl chloride of those oxides that form soluble chlorides do not attain a state of equilibrium as their solubility increases with time and rise in temperature. Organic bases, such as pyridine, quinoline, α-, β-, and γ-picoline, and dimethylaniline, are also soluble in acetyl chloride. The solubility and other properties of individual substances differ much, as seen from Table 1(b).

Titanium tetrachloride, stannic chloride, arsenic trichloride, phosphorus trichloride, phosphorus oxychloride and thiophosphoryl chloride are freely miscible with acetyl chloride. Development of colour when substances are dissolved in acetyl chloride indicates the formation of complexes.[9] Examination of such substances shows that they are either Lewis acids or are capable of producing these after solvolysis, or are bases such as pyridine. The constitution of these solutions is discussed later.

[1] Koehl and Wenzke, *J. Amer. Chem. Soc.*, 1937, **59**, 1418.
[2] Allen and Sutton, *Trans. Faraday Soc.*, 1951, **47**, 236.
[3] (*a*) Phillips, Hunter, and Sutton, *J.*, 1945, 146; (*b*) Skinner, *Trans. Faraday Soc.*, 1945, **41**, 645.
[4] Ketelaar and Palmer, *J. Amer. Chem. Soc.*, 1937, **59**, 2629.
[5] Lewis and Wilkins, *J.*, 1955, 56.
[6] *International Critical Tables*, 1926, **6**, 82.
[7] Schlundt and Germann, *J. Phys. Chem.*, 1925, **29**, 353.

TABLE 1(a). *Solubility (g./100 g. of solvent) of substances in acetyl chloride at* 30° ± 0·1°

Compound	S *	Colour of solution	Heat effect †	Solid phase	Compound	S *	Colour of solution	Heat effect †	Solid phase
$BiCl_3$	15·04	Yellow	0	$BiCl_3$	$ZnCl_2$	7·86	Yellow	0	$ZnCl_2$
$SbCl_3$	150·00	Red	—	$SbCl_3$	$SnCl_4$	Miscible	Yellow	+	
BiOCl	71·80	Dark red	++	BiOCl	$AsCl_3$	Miscible	Colourless	0	
SbOCl	92·13	Orange-yellow	++	SbOCl	$TeCl_4$	8·57	Dark red	+	$TeCl_4$
$SbCl_5$	24·12	Yellow	++	$SbCl_5$,AcCl	$TiCl_4$	Miscible	Yellow	+	
PCl_3	Miscible	Colourless	0		PCl_5	20·92	Colourless	+	PCl_5
$FeCl_3$	27·87	Red	0	$FeCl_3$	$PSCl_3$	Miscible	Colourless	0	
$HgCl_2$	3·12	Pale yellow	+	$HgCl_2$	$POCl_3$	Miscible	Colourless	0	
$SnCl_2$	4·47	Red	0	$SnCl_2$					

TABLE 1(b). (*Qualitative.*)

Compound	S	Colour of solution	Heat effect	Solid phase
Pyridine	Sparingly sol.	Orange-yellow	++	C_5H_5N,AcCl
α-Picoline	Freely sol.	Yellow	+	
β-Picoline	Sparingly sol.	Yellow	++	β-Picoline, AcCl
γ-Picoline	Sparingly sol.	Yellow	+	γ-Picoline, AcCl
Quinoline	Miscible	Pink	+	
Dimethylaniline	Miscible	Violet	+	
Diethylaniline	Miscible	Green	+	
$(C_7H_7NMe_2)Cl$	Sparingly sol.	Colourless	0	$(C_7H_7NMe_2)Cl$
$(C_7H_7NPhMe_2)Cl$	Fairly sol.	Colourless	0	$(C_7H_7NPhMe_2)Cl$
CaO	Insol.		++	CaO,2AcCl
CuO	Insol.		++	$3CuCl_2$,CuO,2AcC
CdO	Insol.		+	CdO
ZnO	Sparingly sol.	Red	++	$ZnCl_2$,2(ZnO,2AcCl)
HgO	Sparingly sol.	Yellow	++	HgO + $HgCl_2$
Sb_2O_5	Fairly sol.	Dark red	0	Sb_2O_5
As_2O_3	Fairly sol.	Nil	0	As_2O_3

* Miscible means freely soluble. Sparingly soluble and fairly soluble signify solubility of about <5% and 15%, respectively.

† 0 = Nil; — = cooling; + = slight; ++ = considerable.

Formation of solvates in acetyl chloride has been known since 1901 when a solvate of aluminium chloride was reported.[8] Conductivity measurements of solutions of ferric chloride in acetyl chloride have indicated the formation of complex ions in solution;[9] but attempts to isolate such a solvate of ferric chloride have failed, probably owing to the catalytic enolization of acetyl chloride. Solvates of boron trifluoride and boron trichloride,[11] and a monosolvate of magnesium bromide[12] are known. Recently Greenwood and Wade[13] reported the formation of a monosolvate of gallium trichloride with acetyl chloride. The formation of a compound of titanium tetrachloride and acetyl chloride in carbon disulphide has been mentioned.[14,15] In the present work, this compound has been prepared by cooling a mixture of titanium tetrachloride and acetyl chloride. Stannic chloride, the solid solvate of which is known with phosphorus oxychloride[16] and selenium oxychloride,[17] does not give any solid solvate with acetyl chloride under ordinary conditions. Similar behaviour has also been noticed with sulphur monochloride[18] with which it is also freely miscible. The existence of its solvate, however, is quite evident from the results of conductivity measurements given below. While studying the properties of liquid sulphur dioxide, Seel[19] isolated a compound of antimony pentachloride with

[8] Boeseken, *Rec. Trav. chim.*, 1901, **20**, 102.
[9] Wertyporoch, Kowalski, and Roeske, *Ber.*, 1933, **66**, 1232.
[10] Adkins and Thompson, *J. Amer. Chem. Soc.*, 1949, **71**, 2242.
[11] Meerwein and Maier-Huser, *J. prakt. Chem.*, 1932, **134**, 51.
[12] Menschutkin, *J. Russ. Phys. Chem. Soc.*, 1907, **39**, 102.
[13] Greenwood and Wade, *J.*, 1956, 1527.
[14] Bertrand, *Bull. Soc. chim. France*, 1880, **33**, 403.
[15] Cullinane, Chard, and Leyshon, *J.*, 1952, 4106.
[16] Garner and Sugden, *J.*, 1929, 1298.
[17] Smith, *Chem. Rev.*, 1938, **23**, 165.
[18] Hamdard, M.Sc. Thesis, 1956.
[19] Seel, *Z. anorg. Chem.*, 1943, **252**, 24.

acetyl chloride. We have prepared this compound by direct interaction of the two components.

Most of the oxides react with acetyl chloride to produce chlorides, but cupric oxide yielded an intermediate of the composition $3CuCl_2,CuO,2AcCl$, as a product of incomplete solvolysis, but calcium oxide gave a disolvate. The solvolytic reactions are discussed separately.

TABLE 2. *Formation of solvates in acetyl chloride.*

Substance	Solvate	M. p.	Substance	Solvate	M. p.
BF_3 [11]	$BF_3,CH_3\cdot COCl$	−70° to −60°	$SbCl_5$ [19]	$SbCl_4,CH_3\cdot COCl$	—
BCl_3 [11]	$BCl_3,CH_3\cdot COCl$	−54°	Pyridine [20]	$C_5H_5N,CH_3\cdot COCl$	98—100°
$MgBr_2$ [12]	$MgBr_2,CH_3\cdot COCl$	—	α-Picoline	$2C_6H_7N,3CH_3\cdot COCl$	61—62°
$AlCl_3$ [8]	$AlCl_3,CH_3\cdot COCl$	—	β-Picoline	$C_6H_7N,CH_3\cdot COCl$	78—80°
$GaCl_3$ [13]	$GaCl_3,CH_3\cdot COCl$	46·5°	γ-Picoline	$C_6H_7N,CH_3\cdot COCl$	125—127°
$TiCl_4$ [14,15]	$TiCl_4,CH_3\cdot COCl$	20·5°			

Dehn [20] reports that solvates and dihydrochlorides are formed simultaneously from bases, pyridine being an exception.[10] The solid solvates of pyridine and of β- and γ-picoline separate spontaneously, but that of α-picoline has been prepared by removing the excess of the solvent. It is apparent from Table 2 that most of the ionic chlorides do not form solvates with acetyl chloride.

Specific conductivities of solutions in acetyl chloride are given in Table 3. As acetyl chloride has a low dielectric constant, no attempt has been made to deduce the dissociation

TABLE 3. *Specific conductivity* (κ) *of acids and bases in acetyl chloride at* 30° ± 0·1°

(Specific conductivity of acetyl chloride, $3·5 \times 10^{-7}$ ohm^{-1} cm.$^{-1}$ at 0°.[23])

Substance	Concn. (mole/l.)	$10^5\kappa$ (ohm^{-1} cm.$^{-1}$)	Substance	Concn. (mole/l.)	$10^5\kappa$ (ohm^{-1} cm.$^{-1}$)
Benzyltrimethylammonium chloride	0·0084	44·50	γ-Picoline	0·0094	6·134
			Quinoline	0·0088	21·8
Benzyldimethylphenylammonium chloride	0·0092	48·60	Dimethylaniline	0·0093	3·569
			Stannic chloride	0·0087	0·3834
α-Picoline	0·0119	8·624	Titanium tetrachloride	0·0089	0·8735
β-Picoline	0·0090	5·707			

constants, etc., quantitatively. However, the results are significant from a qualitative point of view; for the solutions are much more conducting than either the solvent ($\kappa = 3·5 \times 10^{-7}$ at 0° [23]) or the solutes stannic chloride [22] or titanium tetrachloride [21] which are non-conducting liquids.

Formation of conducting solutions can only be explained on the basis of the existence of solvates which behave as ion pairs in acetyl chloride. The Lewis acids, stannic chloride and titanium tetrachloride, are known to tend to form hexachlorostannate [24] and hexachlorotitanate ions.[25] On this basis the structure of their solvates in solutions of acetyl chloride can be represented as follows:

$$TiCl_4,AcCl \rightleftharpoons Ac^+ + TiCl_5^-$$
$$TiCl_4,AcCl + AcCl \rightleftharpoons 2Ac^+ + TiCl_6^{2-}$$
$$SnCl_4 + 2AcCl \rightleftharpoons 2Ac^+ + SnCl_6^{2-}$$

The structure of the solvate of pyridine, by analogy with its solvates in selenium oxychloride [17,26] and phosphorus oxychloride,[27] would be $C_5H_5N,AcCl \rightleftharpoons C_5H_5NAc^+ + Cl^-$. The ionization of the solvates of the picolines, and of solutions of quinoline and

[10] Dehn, *J. Amer. Chem. Soc.*, 1912, **34**, 1399.
[21] Eingorn, *Ukrain. Khim. Zhur.*, 1950, **16**, 404.
[22] *International Critical Tables*, 1926, **6**, 142.
[23] *Ibid.*, p. 143.
[24] Dickinson, *J. Amer. Chem. Soc.*, 1922, **44**, 276.
[25] Rumpf, *Compt. rend.*, 1936, **202**, 950.
[26] Jackson and Smith, *J. Amer. Chem. Soc.*, 1940, **62**, 544.
[27] Gutmann, *Monatsh.*, 1954, **85**, 1077.

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dimethylaniline in acetyl chloride, can be similarly expressed. As these increase the chloride-ion concentration in acetyl chloride solutions, they will act as solvobases in acetyl chloride. On the other hand, the quaternary ammonium chlorides which are soluble in acetyl chloride give highly conducting solutions. These also increase the chloride-ion concentration and will act as ansolvobases.

The behaviour of these compounds as acids or bases is confirmed in Parts III and IV of this series in which the acid–base neutralization reactions have been studied by complex formation as well as conductometrically.

Experimental

Reagents.—Acetyl chloride, b. p. 50—52°, was redistilled over 10% of dimethylaniline and the fraction of b. p. 50·5—51·5° was refractionated over sodium. It was prepared in small quantities as needed. All other substances were dried before use according to standard methods, and in case of doubt, their purity was checked by analysis.

Estimation of Solubility.—Quantities of the anhydrous solids and acetyl chloride were mixed in glass ampoules, the solid being in excess. All transfers of materials were carried out in a dry box and the ampoules were immediately sealed and shaken in a thermostat kept at 30° ± 0·1°, and 40—48 hr. were allowed for equilibrium to be attained. The ampoule was broken, and the solution was quickly filtered through a sintered-glass funnel in the dry. The solubility of the substance was determined either by evaporating a known weight of the saturated solution to dryness in the dry or by determination of the cation from a known weight of the saturated solution.

Preparation of Solvates.—In the preparation of solvates, different substances (*ca.* 5 g.) were shaken in sealed tubes with acetyl chloride (*ca.* 15 g.) for about 24 hr. Care was taken to manipulate acetyl chloride and the anhydrous solids in a dry box. The mixture was filtered through a sintered-glass funnel and the residue was washed with acetyl chloride, a small quantity of dry light petroleum (b. p. 40—60°), and sometimes with carbon tetrachloride, and kept under vacuum to remove volatile solvent. In most of the cases, both solid and solution were examined for solvate.

Monosolvate of Antimony Pentachloride.—The *solvate* (3·5 g. from 4 g. of pentachloride) (Found: Cl, 54·1; Sb, 30·75%; Cl/Sb, 1·8. $SbCl_5,CH_3{\cdot}COCl$ requires Cl, 56·35; Sb, 32·3%; Cl/Sb, 1·75) did not melt but decomposed, had a pungent smell, and was fairly soluble in acetyl chloride and insoluble in light petroleum.

Monosolvate of Titanium Tetrachloride.—After drying in vacuum the *monosolvate* (1·5 g. from 2 ml. of tetrachloride) (Found: Cl, 64·8; Ti, 17·4. $TiCl_4,CH_3{\cdot}COCl$ requires Cl, 66·2; Ti, 17·9%) was very hygroscopic and freely soluble in acetyl chloride.

Monosolvate of Pyridine.—To ice-cold acetyl chloride (10 ml.), pyridine (2 ml.) was added dropwise and the mixture was stirred vigorously till a yellow solid appeared, then kept in an ice-bath for about ½ hr., with exclusion of moisture. This yellow solid was filtered off in a dry atmosphere and dried. The pyridine content was estimated according to Smith and Jackson;[26] nitrogen was computed from these results and chlorine was determined by Volhard's method (Found: Cl, 22·4; N, 8·55. $C_5H_5N,CH_3{\cdot}COCl$ requires Cl, 22·5; N, 8·9%). This *solvate* was hygroscopic and melted at 98—100°. It was sparingly soluble in acetyl chloride.

Solvate of α-Picoline.—α-Picoline (3 ml.) gave a dark yellow solution in acetyl chloride (15 ml.) and on addition of more base (1 ml.) and cooling, an oil separated. Excess of acetyl chloride was removed in a vacuum. A deep red solid was formed which was washed with dry light petroleum (b. p. 40—60°) and kept under vacuum to give the *solvate* (2·8 g.), which was analysed as described under pyridine (Found: Cl, 25·3; N, 6·2. $2C_6H_7N,3CH_3{\cdot}COCl$ requires Cl, 25·3; N, 6·65%). It was a reddish hygroscopic solid, m. p. 61—63°, freely soluble in acetyl chloride.

Monosolvate of β-Picoline.—β-Picoline (1·5 g.) on addition to cold acetyl chloride (15 ml.) gave a rose-coloured solid instantaneously, heat being evolved. This solid, when kept for about 1 hr. in ice and stirred, became a dirty yellow solid, which was filtered off and dried (2·1 g.). It was analysed as already described (Found: Cl, 20·4; N, 7·8. $C_6H_7N,CH_3{\cdot}COCl$ requires Cl, 20·7; N, 8·2%). The *solvate* was a very hygroscopic solid, and under high vacuum

it changed to a dark red liquid. It melted at 77—78° and was sparingly soluble in acetyl chloride.

Monosolvate of γ-Picoline.—γ-Picoline (2 ml.) was added dropwise with stirring to ice-cooled acetyl chloride (15 ml.); an orange-yellow solid separated. The mixture was kept in ice for ½ hr. and then filtered in absence of moisture and kept under moderate vacuum. The *solvate* (1·8 g.), which smelt slightly of acetyl chloride, was analysed as already mentioned (Found: Cl, 20·3; N, 7·85%). This was a hygroscopic solid, m. p. 125—127°, and changed colour under vacuum. It was sparingly soluble in acetyl chloride and almost insoluble in dry light petroleum (b. p. 40—60°).

For resistance measurements we used a bridge-type instrument WBR No. 108 with logarithmic indicator amplifier (Type TAV, IKc, No. 034; Wissenschaftlich-Technische Werkstatten, Wielheim/Oby., Germany).

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56. *Acetyl Chloride as a Polar Solvent. Part II.* Solvolytic Reactions in Acetyl Chloride.*

By RAM CHAND PAUL, DULA SINGH, and SARJIT SINGH SANDHU.

Solvolysis of a number of oxides, carbonates, nitrates, nitrites, acetates, and sulphates has been studied quantitatively in acetyl chloride. A mechanism for the solvolysis of these compounds, based on the ionization of acetyl chloride, has been suggested.

THE literature contains scattered references to the solvolytic properties of acetyl chloride. McGookin and Page [1] used organic acid chlorides and metallic oxides to synthesize the acid anhydrides. Mackenzie and Winter [2] reported formation of acetyl perchlorate from silver perchlorate and acetyl chloride in acetic anhydride. Chrétien and Oechsel [3] prepared pervanadyl chloride, uranyl chloride, and manganese tetrachloride from vanadium pentoxide, uranium trioxide, and manganese dioxide by treating them with acetyl chloride. Recently, a method for the preparation of anhydrous chlorides has been suggested [4] in which hydrated salts of metals are treated with the requisite quantity of acetyl chloride in benzene.

However, the solvolytic properties of acetyl chloride have not hitherto been systematically studied. Most of the anhydrous chlorides are insoluble in acetyl chloride and thus these reactions constitute a very convenient method for their preparation. Oxides, oxychlorides, nitrates, nitrites, acetates, and sulphates are solvolysed by acetyl chloride; the results are given in the Table. The calcium oxide solvate when heated at 150° gives an equimolecular mixture of calcium chloride and calcium oxide. At higher temperatures an equilibrium is set up due to the back reaction,[5] *i.e.*, formation of acetyl chloride from calcium chloride and acetic anhydride.

Antimony and bismuth oxychlorides formed solvates of the corresponding trichloride and acetic anhydride. The constitution of these solvates was proved by comparison of their α-picoline complexes with those made directly from the corresponding trichloride and α-picoline in acetyl chloride.

Tellurium dioxide and acetyl chloride gave only a solution from which a mixture of

* Part I, preceding paper.

[1] McGookin and Page, *J.*, 1951, 2769.
[2] Mackenzie and Winter, *Trans. Faraday Soc.*, 1948, **44**, 159.
[3] Chrétien and Oechsel, *Compt. rend.*, 1938, **206**, 254.
[4] Watt, Gentile, and Helvenston, *J. Amer. Chem. Soc.*, 1955, **77**, 2752.
[5] Gmunder, *Helv. Chim. Acta*, 1953, **36**, 2021.

products was obtained on removal of solvent. Morgan and Drew [6] reported formation of acids from tellurium tetrachloride and acetic anhydride, which could be the initial products of solvolysis of the dioxide.

Compound	Solvolysed product	Colour of product	Temp.	Time (hr.)	Analysis % Found	% Calc.
CuO	$CuO,3CuCl_2,2AcCl$	Brown	Room	24	Cl 38·0	38·4
					Cu 34·8	34·3
	$CuCl_2$	,,	Reflux	8	Cl 51·1	52·8
					Cu 46·1	47·2
HgO	$HgCl_2$	White	Room	~500	Cl 25·3	26·2
					Hg 72·1	73·8
	$HgCl_2$	,,	Reflux	9	Cl 25·7	26·0
					Hg 71·2	73·8
SeO_2	$SeCl_4$	Light yellow	Room	20	Cl 63·5	64·25
					Se 35·25	35·75
CaO	$CaO,2AcCl$	White	Room	24	Cl 33·5	33·3
					Ca 18·7	18·8
	$CaO,CaCl_2$	,,	Reflux	12	Cl 43·4	43·1
ZnO	$3ZnCl_2,2Ac_2O$	Reddish-brown *	Room	24	Cl 34·8	34·8
					Zn 31·7	31·9
Fe_2O_3	$2FeCl_3,3Ac_2O$	Reddish-brown *	Reflux	4	Cl 35·8	33·8
					Fe 18·5	17·8
Bi_2O_3	$2BiCl_3,Ac_2O$	Dark red	Room	24	Cl 29·65	29·1
					Bi 56·65	57·0
Sb_2O_5	$2SbCl_5,5Ac_2O$	Dark red	Room	24	Cl 32·1	32·0
					Sb 21·6	22·1
BiOCl	$BiCl_3,Ac_2O$	Dark red *	Room	24	Cl 25·6	25·5
					Bi 50·2	50·1
SbOCl	$SbCl_3,Ac_2O$	Orange-yellow †	Room	24	Cl 32·2	32·3
					Sb 37·2	36·85
$AgNO_3$	AgCl	White	Reflux	3	Ag 73·6	75·3
KNO_3	KCl	White	Reflux	3	Cl 45·4	47·0
$NaNO_3$	NaCl	White	Reflux	2	Cl 57·9	60·7
$Hg(AcO)_2$	$HgCl_2$	Brown	Reflux	8	Cl 23·9	26·2
					Hg 70·0	73·8
$CuCO_3$	$CuCl_2$	Brown	Reflux	6	Cl 50·7	52·8
					Cu 45·7	47·2
$CdCO_3$	$CdCl_2,Ac_2O$	Yellow	Reflux	8	Cl 30·65	30·3
					Cd 47·9	47·9
$HgSO_4$	$4HgCl_2,HgSO_4$	Dirty white	Reflux	12	Cl 20·5	20·9
					Hg 70·4	72·5

* Viscous liquid. † Liquid.

Note: Where results for chlorine or metals are low, the possibility of incomplete solvolysis due to the formation of a protective layer of the insoluble chloride on the unsolvolysed product is presumed, and certain chlorides contain some inert matter formed as a result of side reactions.

Aluminium oxide resists solvolysis in acetyl chloride, and lead dioxide is solvolysed very slowly.

The solvolysis of silver nitrate in benzoyl chloride has been reported.[7] In acetyl chloride it is slowly converted into silver chloride, reaction being retarded by the insolubility of the reagents and the formation on it of a layer of silver chloride. At room temperature, copious brown fumes of oxides of nitrogen are evolved, but to ensure completion of the reaction, the reactants were refluxed for 3 hr.

Acetyl chloride is believed to ionize thus: $AcCl \rightleftharpoons Ac^+ + Cl^-$.[8] The mode of these solvolytic reactions in acetyl chloride can then be expressed as follows:

$$AgNO_3 \rightleftharpoons Ag^+ + NO_3^- \text{ (slightly soluble and feebly ionized)}$$

$$Ac^+ + Cl^- + Ag^+ + NO_3^- \longrightarrow AgCl + AcNO_3$$

[6] Morgan and Drew, *J.*, 1925, **127**, 531.
[7] Francis, *Ber.*, 1906, **39**, 3798.
[8] Preceding paper; Paul and Sandhu, *Proc. Chem. Soc.*, 1957, 262.

Acetyl nitrate formed during this reaction may decompose to produce nitrogen dioxide or nitrosyl chloride and other products in the presence of excess of acetyl chloride: [9]

$$4AcNO_3 \longrightarrow 2Ac_2O + 4NO_2 + O_2$$
$$2AcNO_3 + 6AcCl \longrightarrow 4Ac_2O + 2NOCl + 2Cl_2$$

Carbonates and nitrites are similarly solvolysed, carbon dioxide and oxides of nitrogen being evolved.

Mercuric acetate reacts to produce mercuric chloride and acetic anhydride: $Hg^{++} + 2AcO^- + 2Ac^+ + 2Cl^- \longrightarrow HgCl_2 + 2Ac_2O$. McGookin and Page [1] assumed that the primary reaction between an oxide and an acid chloride is the formation of an addition compound which rearranges to produce acid anhydride and metallic chloride: $SeO_2 + 4AcCl \longrightarrow SeO_2,4AcCl \longrightarrow SeCl_4 + 2Ac_2O$. In certain cases the addition product of acetic anhydride and metallic chloride is obtained: $Fe_2O_3 + 6AcCl \longrightarrow Fe_2O_3,6AcCl \longrightarrow 2FeCl_3,3Ac_2O$. The existence of an intermediate compound has been shown in the case of incomplete solvolysis of cupric oxide (see above) and supports these views.

Experimental

Reagents.—Acetyl chloride was prepared and stored as described in the preceding paper. Oxides and other salts were dried before use and, if necessary, to remove traces of moisture and carbonate, the oxide was heated to an appropriate temperature. A dry box and calcium chloride guard-tubes were used to avoid contact of the reactants with damp air.

General Procedure.—Compounds could be partially solvolysed by keeping a mixture with enough acetyl chloride in a sealed ampoule at room temperature for a few days. In some cases the solvolysis went to completion even at room temperature but more often, to attain complete or maximum solvolysis, the following procedure was adopted: Well-dried solid (3·5 g.) was added to acetyl chloride (30 ml.) and the mixture was refluxed with the exclusion of moisture for 4—12 hr. and acetyl chloride was occasionally replenished. The solid was filtered off, washed with dry light petroleum (b. p. 40—60°), kept under vacuum, and analysed.

Sometimes the solvolyzed product went into solution, from which it was isolated either by addition of solvents such as dry light petroleum and carbon tetrachloride, or by removal of excess of solvent. The product so obtained was analysed by following the usual procedure. If the solvolysed product was liquid, it was purified by repeated washing with dry light petroleum and keeping it under vacuum.

Reaction of Zinc Chloride with Acetic Anhydride.—Zinc chloride (4 g.) was refluxed with acetic anhydride (20 ml.) for 3 hr. A dark red solution, similar to one obtained from zinc oxide and acetyl chloride, was formed; this solution was distilled under reduced pressure (45 mm.) at 120° to remove the excess of acetic anhydride. The residual liquid was washed and stored (as above) before analysis (Found: Cl, 29·0. $ZnCl_2,Ac_2O$ requires Cl, 29·8%).

This *compound* was then heated on an oil-bath at 150° under reduced pressure; heating was stopped when gas evolution ceased, and the sample was analysed (Found: Cl, 34·5; Zn, 31·6. $3ZnCl_2,2Ac_2O$ requires Cl, 34·8; Zn, 31·9%).

Reaction of Antimony Pentachloride with Acetic Anhydride.—Antimony pentachloride (2 ml.) was added dropwise to ice-cold acetic anhydride (5 ml.); heat was evolved and a dark red solution obtained. This liquid was thoroughly washed with carbon tetrachloride and kept under vacuum (Found: Cl, 30·35; Sb, 20·5. $SbCl_5,3Ac_2O$ requires Cl, 29·3; Sb, 20·1%). This dark red, thick liquid was kept under vacuum for about a week. The viscous liquid so obtained was analysed (Found: Cl, 32·7. $2SbCl_5,5Ac_2O$ requires Cl, 32·0%).

Solvolysis of Bismuth Oxychloride.—A compound BiOCl,2AcCl was obtained from bismuth oxychloride or bismuth oxide with acetyl chloride. It can also be represented as $BiCl_3,Ac_2O$, and this structure was confirmed by the following experiment.

Reaction with α-picoline. To the compound (4 g.) in acetyl chloride (10 ml.), α-picoline (1 g.) in acetyl chloride (10 ml.) was added dropwise. The solution was triturated and the yellowish crystals were washed with acetyl chloride, followed by light petroleum, and kept under vacuum (yield, 4 g.) (Found: Cl, 31·0; Bi, 37·55. $[C_6H_7NAc]BiCl_4,AcCl$ requires Cl, 31·4; Bi, 37·0%).

[9] Diels and Okada, *Ber.*, 1911, **44**, 3333.

Its m. p. (91°) was not depressed on mixing with the sample obtained directly by the interaction of bismuth trichloride and α-picoline in acetyl chloride.

Solvolysis of Antimony Oxychloride.—A compound, $SbOCl,2AcCl$ or $SbCl_3,Ac_2O$, was similarly treated with α-picoline; the resulting reddish liquid was triturated with three portions of acetyl chloride, and yellowish-brown solid obtained, m. p. 94° (Found: Cl, 36·9; Sb, 25·4. $[C_6H_7NAc]SbCl_4,AcCl$ requires Cl, 37·1; Sb, 25·4%). An identical *compound* (mixed m. p.) was obtained by the interaction of antimony trichloride and α-picoline in acetyl chloride.

Solvolysis of Bismuth Oxide.—Bismuth oxide yielded crystalline $BiO,BiCl_4,2AcCl$ or $2BiCl_3,Ac_2O$ together with a product similar to that obtained from bismuth oxychloride in solution. The following experiments were performed to decide the nature of present product.

Supposed reaction of bismuth trichloride with bismuth oxychloride. Dry bismuth oxychloride (2 g.) was added to a saturated solution (15 ml.) of bismuth trichloride in acetyl chloride. A reddish solution was obtained and heat was evolved, but no solid separated on chilling or overnight. This solution, on addition of dry light petroleum (b. p. 40—60°), gave only a liquid resembling the product obtained from bismuth oxide and acetyl chloride in the liquid phase.

Reaction of bismuth trichloride with acetic anhydride. Dry bismuth trichloride (30 g.) and acetic anhydride (25 ml.) were refluxed for 7 hr. to give a thick, dark red liquid which was washed with dry carbon tetrachloride and kept under vacuum (Found: Cl, 24·7; Bi, 53·7. Calc. for $BiCl_3,Ac_2O$: Cl, 25·4; Bi, 50·1%. Calc. for $BiCl_2OAc$: Cl, 20·9; Bi, 60·65%). The solvolysis of bismuth trichloride in acetic anhydride has been reported,[10] but the failure of the first reaction and a partial success of this one lead to the probability that the product is $BiCl_3,Ac_2O$ contaminated with a little $BiCl_2OAc$.

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[10] Schmidt, Blohm, and Jander, *Angew. Chem.*, 1947, **59**, 233.

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57. *Acetyl Chloride as a Polar Solvent. Part III.*[1] *Formation of Acid–Base Neutralization Complexes in Acetyl Chloride.*

By (MISS) KAMLA GOYAL, RAM CHAND PAUL, and SARJIT SINGH SANDHU.

Titanium tetrachloride, stannic chloride, zirconium tetrachloride, and tellurium tetrachloride, which act as solvoacids in acetyl chloride, react with ansolvobases (benzyltrimethylammonium chloride and benzyldimethylphenylammonium chloride) and solvobases (quinoline, α-picoline, and dimethylaniline) to yield the acid–base neutralization complexes in acetyl chloride. The mode of their formation and the constitution of acidic and basic solutions in acetyl chloride are discussed.

DISSOCIATION of acetyl chloride, $AcCl \rightleftharpoons Ac^+ + Cl^-$, is supported by study of solubilities, solvate formation, and solvolytic reactions in it.[1-4] According to modern theory of acids and bases,[5] those substances which increase the concentration of the acetylium ions and of chloride ions, respectively, are acids and bases in acetyl chloride solution. The formation of solvates by Lewis acids and organic tertiary bases, and the conductivity of their solutions, have indicated the existence of acidic and basic species in this solvent.[3] Owing to their strong tendency to acquire a higher covalency by combining with chloride ions,[5,6] the Lewis acids indirectly increase the concentration of acetylium ions and thus will act as solvoacids in acetyl chloride.

Organic tertiary bases such as pyridine and quinoline can combine with acetylium ions to form acetylpyridinium and acetylquinolinium ions. Thus, they indirectly increase the concentration of the chloride ions in acetyl chloride and will act as solvobases.

[1] Part II, preceding paper.
[2] Paul and Sandhu, *Proc. Chem. Soc.*, 1957, 262.
[3] Paul, Singh, and Sandhu, Part I, *J.*, 1959, 315.
[4] Manhas, Paul, and Sandhu, Part IV, following paper.
[5] Smith, *Chem. Rev.*, 1938, **23**, 165.
[6] Gutmann, *Monatsh.*, 1954, **85**, 404.

On the other hand, the quaternary ammonium chlorides which are soluble in acetyl chloride will directly increase the chloride-ion concentration in solution and therefore act as ansolvobases. As the chlorides of alkali and alkaline-earth metals are insoluble in acetyl chloride, benzyltrimethylammonium and benzyldimethylphenylammonium chlorides, which are more soluble than tetramethylammonium chloride, have been used as ansolvobases to study the neutralization reactions with the Lewis acids titanium tetrachloride, stannic chloride, zirconium tetrachloride, and tellurium tetrachloride.

Both of these quaternary ammonium chlorides react with these Lewis acids in acetyl chloride when mixed in a molar ratio of 2 : 1 to yield insoluble crystalline precipitates of the type $[NR^1{}_3R^2R^3]_2MCl_6$ (M = Ti, Sn, Zr, or Te). The precipitation of these complexes can be explained on the basis of the formation of solvoacids by the four Lewis acids in acetyl chloride. Titanium tetrachloride, which forms a monosolvate in acetyl chloride and gives conducting solutions,[3] can be regarded as existing in solution as $TiCl_4,AcCl + AcCl \rightleftharpoons 2Ac^+ + TiCl_6^{2-}$.

Stannic chloride gives conducting solutions in acetyl chloride.[3] Therefore, on the basis of the formation of hexachlorostannate ions,[7] its ionization in acetyl chloride can be represented as $SnCl_4 + 2AcCl \rightleftharpoons 2Ac^+ + SnCl_6^{2-}$. Although the conductivities of zirconium tetrachloride and tellerium tetrachloride solutions in acetyl chloride have not been measured, yet from their general behaviour,[8,9] one can predict the existence of acetylium ions in their solutions in exactly the same way.

The formation of the neutralization complexes between Lewis acids and quaternary ammonium chlorides is due to combination of Ac^+ and Cl^- ions to give only feebly ionized acetyl chloride. A typical neutralization reaction in acetyl chloride can be represented as $2QCl + Ac_2MCl_6 \longrightarrow Q_2MCl_6 + 2AcCl$. In these complexes the ratio of the Lewis acid to the base is 1 : 2, so they are regarded as normal salts. On addition of an excess of the acid solution, the complex dissolves completely when the acid to base molar ratio is 1 : 1. This has been noticed with the complexes of titanium tetrachloride and stannic chloride, and may be attributed to the formation of very soluble acid salts. The formation of an acid salt by the dissolution of the normal salt can be expressed as $Q_2MCl_6 + Ac_2MCl_6 \longrightarrow 2QMCl_6Ac$. The existence of the acid and the normal salts of benzyltrimethyl- and benzyldimethylphenyl-ammonium chlorides with titanium tetrachloride and stannic chloride has been proved conductometrically.[4]

Quinoline acts as a solvobase as indicated by the high specific conductivity of its solutions in acetyl chloride.[3] It forms two complexes with titanium tetrachloride in acetyl chloride. The normal salt, $[C_9H_7NAc]_2TiCl_6$, loses acetyl chloride under vacuum, giving the desolvated complex, $(C_9H_7N)_2TiCl_4$. The acid salt $[C_9H_7NAc]AcTiCl_6$, has been isolated in the partly desolvated form $[C_9H_7NAc]TiCl_5$. The formation of these complexes can be represented as under:

$$B + AcCl \longrightarrow (B,Ac)^+ + Cl^- \quad . . . . . (1)$$

$$2B,AcCl + Ac_2MCl_6 \longrightarrow [(B,Ac)_2MCl_6 + 2AcCl \quad . . . . . (2)$$

$$(B,Ac)_2MCl_6 - 2AcCl \longrightarrow B_2MCl_4 \quad . . . . . (3)$$

$$(B,Ac)_2MCl_6 + Ac_2MCl_6 \longrightarrow 2(B,Ac)AcMCl_6 \quad . . . . . (4)$$

$$(B,Ac)AcMCl_6 - AcCl \longrightarrow (B,Ac)MCl_5 \quad . . . . . (5)$$

The formation of the acid and the normal salt by quinoline with titanium tetrachloride in acetyl chloride has been verified conductometrically.[4]

Quinoline and zirconium tetrachloride, both dissolved in acetyl chloride, react to yield a white precipitate which is considered to be an equimolecular mixture of the normal and the acid salt, $(C_9H_7NAc)_3Ac(ZrCl_6)_2$. This complex is invariably formed when the acid solution is added to the base in acetyl chloride. Quinoline also reacts with tellurium

[7] Dickinson, *J. Amer. Chem. Soc.*, 1922, **44**, 276.
[8] Gutmann and Himml, *Z. anorg. Chem.*, 1956, **287**, 199.
[9] Groeneveld and Zuur, *Rec. Trav. chim.*, 1953, **72**, 617.

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tetrachloride in acetyl chloride when equimolecular solutions of the two are mixed, to form $(C_9H_7NAc)TeCl_5$. All these complexes smell of acetyl chloride; being hygroscopic, their m. p.s could not be determined.

α-Picoline, a stronger base than pyridine, forms a solid solvate with acetyl chloride. With titanium tetrachloride it yields a precipitate of the composition $(C_6H_7N)_2TiCl_4$ which is the completely desolvated normal complex. α-Picoline also reacts with stannic chloride when equimolecular quantities of the two substances are mixed in acetyl chloride. On chilling the mixture and adding dry light petroleum (b. p. 40—60°), a precipitate of $(C_6H_7NAc)AcSnCl_6,AcCl$ has been obtained. The formation of these complexes of α-picoline with titanium tetrachloride and stannic chloride follows the general equations (2)—(4).

Although dimethylaniline does not form a solid solvate with acetyl chloride, it yields conducting solutions.[3] It reacts with titanium tetrachloride in acetyl chloride to yield a complex, $(C_8H_{11}N)_2TiCl_4,AcCl$, and with stannic chloride forms a complex, $(C_8H_{11}N)_2SnCl_4,AcCl$, as expressed by the general equation (2) followed by a partial desolvation: $(B{\cdot}Ac)_2MCl_6 - AcCl \longrightarrow B_2MCl_4,AcCl$. The formation of all these complexes has been confirmed conductometrically.[4]

Experimental

Reagents.—Acetyl chloride was purified as described in previous papers. Titanium tetrachloride and stannic chloride were treated with copper turnings and tin pieces, respectively, and fractionated in a current of dry nitrogen, fractions of b. p. 130°/745 mm. and 112·5—113°/743 mm. respectively being collected. Tellurium tetrachloride was resublimed before use. Zirconium tetrachloride supplied by Messrs. Johnson Matthey & Co. Ltd., London, was used as received.

The quaternary ammonium chlorides were recrystallized from lime-dried alcohol, and the purity of the dried samples was checked by analysis. The organic tertiary bases were fractionally distilled over potassium hydroxide pellets in a current of dry nitrogen and the fractions boiling at the following temperatures were collected: α-picoline, 125·5—126·5°/735 mm.; quinoline, 228—230°/740 mm.; dimethylaniline, 193—194°/736 mm.

Transfers of materials were carried out in a dry box and exposure was kept to a minimum. Filtrations were carried out in sintered-glass funnels in a dry atmosphere, and samples were kept under vacuum before analysis.

Complex	Colour	M. p.†	Metal (%) Found	Metal (%) Calc.	Chlorine (%) Found	Chlorine (%) Calc.	Nitrogen (%) Found	Nitrogen (%) Calc.
$[(CH_3)_2N{\cdot}C_7H_7]_2TiCl_6$	Yellow	165—170°	8·05	8·6	37·8	38·0	4·5	5·0
$[(CH_3)_2N{\cdot}C_7H_7]_2SnCl_6$	White	200—204	18·7	18·8	33·0	33·7	4·1	4·4
$[(CH_3)_2N{\cdot}C_7H_7]_2ZrCl_6$	White	285—290	14·2	14·4	35·3	35·3	4·4	4·6
$[(CH_3)_2N{\cdot}C_7H_7]_2TeCl_6,\frac{1}{2}CH_3{\cdot}COCl$	Yellow	214	18·7	18·8	33·7	33·9	4·4	4·4
$[(CH_3)_2N{\cdot}C_6H_5(C_7H_7)]_2TiCl_6$	Yellow	175—180	7·4	7·0	31·2	31·1	3·8	4·1
$[(CH_3)_2N{\cdot}C_6H_5(C_7H_7)]_2SnCl_6,CH_3{\cdot}COCl$	White	214	14·8	14·2	29·7	29·8	3·6	3·8
$[(CH_3)_2N{\cdot}C_6H_5(C_7H_7)]_2ZrCl_6$	White	115—116	12·9	12·55	29·2	29·25	3·55	3·8
$[(CH_3)_2N{\cdot}C_6H_5(C_7H_7)]_2TeCl_6$	Yellow	170—185	16·7	16·7	28·3	27·85	3·45	3·7
$[C_9H_7N{\cdot}CH_2{\cdot}CO]_2TiCl_6,\frac{1}{2}CH_3{\cdot}COCl$	Yellow	186	7·3	7·45	35·8	35·8	3·9	4·35
$[C_9H_7N]_2TiCl_4$ *	Light yellow	—	10·5	10·7	31·3	31·7	5·9	6·25
$[C_9H_7N{\cdot}CH_2{\cdot}CO]TiCl_3$	Yellow	‡	12·05	12·3	44·9	45·5	3·6	3·6
$[C_9H_7N{\cdot}CH_2{\cdot}CO]_2[CH_2{\cdot}CO][ZrCl_6]_2$	White	‡	15·85	15·6	36·5	36·5	3·4	3·6
$[C_9H_7N{\cdot}CH_2{\cdot}CO]TeCl_5$	Yellow	‡	26·75	26·7	37·2	37·3	2·9	2·9
$[C_9H_7N{\cdot}CH_2{\cdot}CO][CH_2{\cdot}CO]SnCl_6,CH_3{\cdot}COCl$	Orange-yellow	‡	19·7	20·1	42·2	42·3		
$[C_9H_7N]_2TiCl_4$	Orange	135	12·4	12·8	37·25	37·8		
$[C_9H_{11}N]_2TiCl_4,CH_3{\cdot}COCl$	Yellow	‡	9·6	9·4	34·2	34·8		
$[C_9H_{11}N]_2SnCl_4,CH_3{\cdot}COCl$	Dirty white	‡	20·9	20·35	30·6	30·9		

* This was obtained by keeping the preceding compound in a vacuum for 48 hr.
† All with decomposition. ‡ Hygroscopic.

General Procedure for the Preparation of Complexes of Quaternary Ammonium Chlorides.—The normal complexes of different acids with quaternary ammonium chlorides were prepared by adding solutions of the acids to solutions of quaternary ammonium chlorides in acetyl chlorides. The amounts of acids and quaternary ammonium chlorides were in a molar ratio of 1 : 2. Owing to their sparing solubility, the normal complexes separated out and after ½ hr. in an ice-bath were filtered off, washed with acetyl chloride, and dried in a vacuum.

Preparation of Complexes of Organic Tertiary Bases.—The normal complexes of organic tertiary bases and the acids were prepared according to the procedure given for the complexes of quaternary ammonium chlorides. For preparation of acid salts, the solution of the base was added to that of 1 mol. of the acid. On account of their high solubility, the acid salts were generally precipitated by addition of dry light petroleum (b. p. 40—60°). The mixture was kept at a low temperature, and the complex filtered off in absence of moist air and kept in a vacuum desiccator before analysis.

Nitrogen in salts of quaternary ammonium chlorides was determined commercially, that in the remaining samples was determined by Jackson and Smith's method.[10]

The formation of the complexes (except those of tellurium and zirconium tetrachloride) has been confirmed conductometrically.

PANJAB UNIVERSITY, HOSHIARPUR, INDIA. [*Received, April 2nd*, 1958.]

[10] Jackson and Smith, *J. Amer. Chem. Soc.*, 1940, **62**, 544.

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58. *Acetyl Chloride as a Polar Solvent. Part IV.*[1] *Conductometric Titrations in Acetyl Chloride.*

By BALDEV SINGH MANHAS, RAM CHAND PAUL, and SARJIT SINGH SANDHU.

The existence of solvoacids, solvobases, and ansolvobases in acetyl chloride, as already postulated, is confirmed conductometrically. The breaks in the curves correspond to acid : base molar ratios of 1 : 1 and 1 : 2, indicating the formation of normal and acid salts. Most of the complexes recorded in Part III are confirmed, and their formation is explained on the basis of the existence of ionic species in the solutions in acetyl chloride.

THE formation of acid–base neutralisation complexes which have been isolated and analysed as described in Part III[1] has been confirmed conductometrically and the existence of acidic and basic species in acetyl chloride has been indicated. Lewis acids such as stannic chloride[2] and titanium tetrachloride,[3] in the pure state, are non-conducting liquids but their solutions in acetyl chloride[4] are more conducting than the solvent itself ($\kappa = 3{\cdot}5 \times 10^{-7}$ ohm^{-1} at 0°;[5] cf. water, 4×10^{-8} ohm^{-1} at 18°). Similar observations have been recorded for solutions containing solvobases such as pyridine, picolines, quinoline, and dimethylaniline, and ansolvobases such as benzyltrimethylammonium and benzyldimethylphenylammonium chlorides. The mode of ionisation of solutions of all these compounds in acetyl chloride has already been indicated.[4]

Addition of titanium tetrachloride solution to a solution of benzyltrimethylammonium chloride in acetyl chloride results in separation of a light yellow solid, accompanied by a decrease in the conductance of the solution until it reaches a minimum at an acid : base molar ratio of 1 : 2 (Fig. 1), at which the precipitation is complete. On further addition of the acid solution, the precipitate begins to dissolve and the conductance shows a sharp increase. The second break appears when the molar ratio of the acid to base is 1 : 1 and the dissolution of the precipitate is almost complete. Further addition causes no appreciable increase in conductance, and no other break in the curve is observed.

[1] Part III, preceding paper.
[2] *International Critical Tables*, 1926, **6**, 142.
[3] Eingorn, *Ukrain khim. Zhur.*, **16**, 404 (1950).
[4] Paul, Singh, and Sandhu, Part I, *J.*, 1959, 315.
[5] *Op. cit.*, ref. 6, p. 143.

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FIG. 1. FIG. 2. FIG. 3.

FIG. 1. *A, Stannic chloride* (0·01980 *mole*/100 *ml.*) *and benzyltrimethylammonium chloride* (0·0448 *g.*).
B, Titanium tetrachloride (0·03575 *mole*/100 *ml.*) *and benzyltrimethylammonium chloride* (0·0860 *g.*).

FIG. 2. *A, Stannic chloride* (0·01476 *mole*/100 *ml.*) *and benzyldimethylphenylammonium chloride* (0·0502 *g.*).
B, Titanium tetrachloride (0·01619 *mole*/100 *ml.*) *and benzyldimethylphenylammonium chloride* (0·0698 *g.*).

FIG. 3. *A, Stannic chloride* (0·02551 *mole*/100 *ml.*) *and α-picoline* (0·0246 *g.*).
B, Titanium tetrachloride (0·04494 *mole*/100 *ml.*) *and α-picoline* (0·02965 *g.*).

FIG. 4.

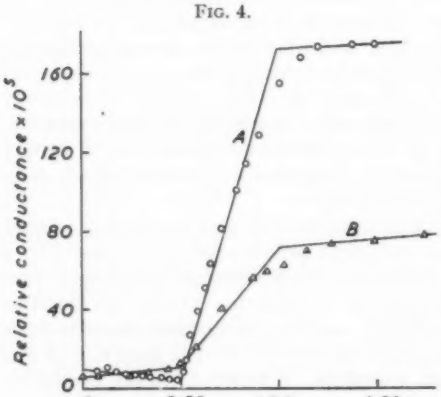

FIG. 5.

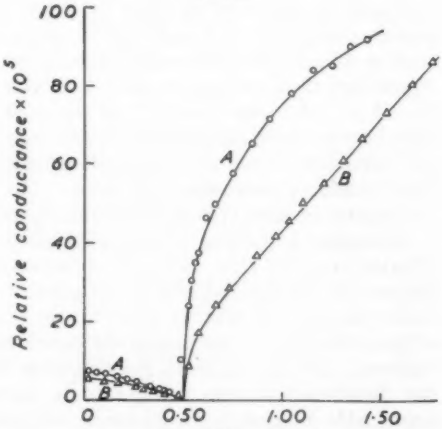

FIG. 4. *A, Stannic chloride* (0·0284 *mole*/100 *ml.*) *and β-picoline* (0·0578 *g.*).
B, Titanium tetrachloride (0·03510 *mole*/100 *ml.*) *and β-picoline* (0·0262 *g.*).

FIG. 5. *A, Stannic chloride* (0·01751 *mole*/100 *ml.*) *and pyridine* (0·0462 *g.*).
B, Titanium tetrachloride (0·02966 *mole*/100 *ml.*) *and pyridine* (0·0246 *g.*).

These results may be interpreted in terms of the existence of ionic species in the solutions.[1,4] Titanium tetrachloride yields a solvate with acetyl chloride which ionises in solution as $TiCl_4,AcCl + AcCl \rightleftharpoons 2Ac^+ + TiCl_6^{2-}$. Similarly with benzyltrimethylammonium chloride in acetyl chloride the appearance of the precipitate is attributed to formation of the hexachlorotitanate: $2Q^+ + 2Cl^- + Ac_2TiCl_6 \longrightarrow Q_2TiCl_6 + 2AcCl$. Hence, progressive removal of benzyltrimethylammonium and chloride ions from the solution results in a decrease in its conductance until precipitation is complete. Dissolution of the precipitate, accompanied by an increase in conductance, can be attributed to the formation and subsequent ionisation of the acid salt: $Q_2TiCl_6 + Ac_2TiCl_6 \longrightarrow 2QTiCl_6Ac \rightleftharpoons 2Ac^+ + 2[QTiCl_6]^-$.

As the acid salt $QTiCl_6Ac$ is more strongly ionised than Q_2TiCl_6 or Ac_2TiCl_6, its progressive formation results in an enormous increase in the conductivity of the solution. Once dissolution is complete, the conductance is scarcely affected by any further addition of the acid which itself is comparatively feebly ionised.

The results of observations in the titrations of the quaternary ammonium chlorides with titanium tetrachloride and stannic chloride are presented in Figs. 1 and 2, which show the characteristics described above. It is noteworthy that the neutralisation complexes of stannic chloride are more soluble in acetyl chloride and hence more conducting than those of titanium tetrachloride. The four compounds concerned have been isolated and identified,[1] but the corresponding acid salts are too soluble to be isolated.

α- and β-Picoline [7] and pyridine [2,6] have also been used for the conductometric titrations with stannic chloride and titanium tetrachloride in acetyl chloride. These bases form solvates [4] and a study of the conductivity of their solutions has shown that they ionise in acetyl chloride as $B + AcCl \longrightarrow B,AcCl \rightleftharpoons (BAc)^+ + Cl^-$. The results of the titration of α-picoline with titanium tetrachloride are presented in Fig. 3; the titrations closely follow the course described above for quaternary ammonium chlorides, the equations being: $2(BAc)^+ + Cl^- + Ac_2MCl_6 \longrightarrow (BAc)_2MCl_6 + 2AcCl$; $(BAc)_2MCl_6 + Ac_2MCl_6 \longrightarrow 2BAc,MCl_6,Ac \rightleftharpoons 2(BAc,MCl_6)^- + 2Ac^+$.

Stannic chloride and α-picoline in acetyl chloride behave analogously (Fig. 3). The acid salt has been isolated and analysed.[1]

Similar titrations of β-picoline and pyridine with titanium tetrachloride and stannic chloride are represented in Figs. 4 and 5. The novel feature about the titration of β-picoline with titanium tetrachloride is that both the normal and the acid salt are soluble; owing to the solubility and slight ionisation of the normal salt, the conductivity of the solution increases slightly up to the point of first inflection (Fig. 4). Then there is a sharp increase in the conductance due to the formation and ionisation of the acid salt. The titration of β-picoline with stannic chloride (Fig. 4) is, however, quite similar to the titrations of α-picoline already discussed.

In pyridine the titration curves obtained with the two acids (Fig. 5) show only one break, corresponding to the formation of normal salt. There is an increase in conductance due to the formation of the acid salt but the precipitate does not dissolve completely, even on addition of a further mole of acid per mole of base, so a second break is not observed.

Quinoline and dimethylaniline are freely miscible with acetyl chloride and do not form any solid solvate under ordinary experimental conditions. The existence of their solvates in solutions is, however, clearly indicated by the high specific conductivities of their solutions.[4] On the addition of a solution of quinoline to one of titanium tetrachloride in acetyl chloride, the conductance rises to a maximum at a point corresponding to a base : acid molar ratio of 1 : 1 (Fig. 6). Further addition of the base solution results in separation of a yellow precipitate and the conductance of the solution slowly decreases. At the molar ratio 2 : 1, a second break in the curve appears; further addition of base

[6] Gutmann, *Monatsh.*, 1954, **85**, 1077.
[7] Henery, Hazel, and McNabb, *Analyt. Chim. Acta*, 1956, **15**, 187.

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then has only a slight effect on the conductance. The first two portions of the curve can be attributed to the successive processes

$$BAc)^+ + Cl^- + 2AcTiCl_4 \longrightarrow BAc,TiCl_4{\cdot}Ac + AcCl \rightleftharpoons (BAc,TiCl_4)^- + Ac^+$$
$$(BAc,TiCl_4)^- + Ac^+ + (BAc)^+ + Cl^- \longrightarrow (BAc)_2TiCl_4 + AcCl$$

The slight increase beyond the second break is due to addition of the comparatively weakly ionised base. In this titration acid salt begins to separate just before the molar ratio 1 : 1 is attained, so the relevant points do not fall on a regular curve. The two neutralisation complexes formed by quinoline with titanium tetrachloride have been isolated and analysed.[1]

FIG. 6.

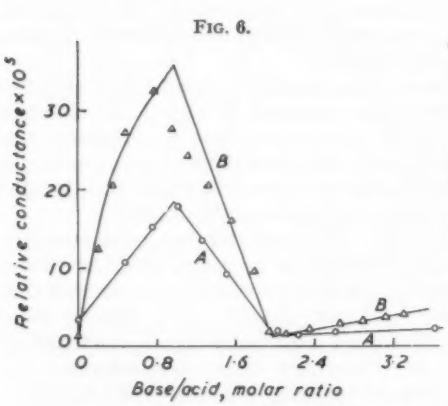

FIG. 7.

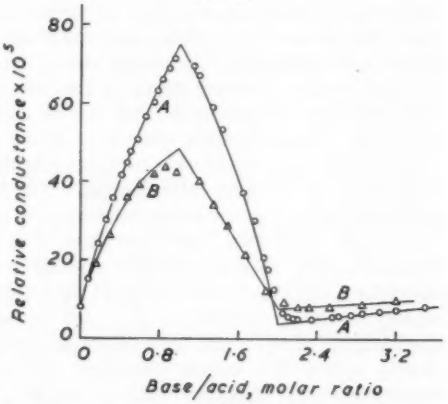

FIG. 6. *A, Quinoline* (0·02917 *mole*/100 *ml.*) *and stannic chloride* (0·0090 *g.*).
B, Quinoline (0·0443 *mole*/100 *ml.*) *and titanium tetrachloride* (0·0240 *g.*).

FIG. 7. *A, Dimethylaniline* (0·02655 *mole*/100 *ml.*) *and stannic chloride* (0·0702 *g.*).
B, Dimethylaniline (0·0352 *mole*/100 *ml.*) *and titanium tetrachloride* (0·0436 *g.*).

The curve obtained for the titration of quinoline against stannic chloride is similar to that just discussed and indicates the formation of both an acid and a normal salt.

The course of neutralisation of titanium tetrachloride and stannic chloride with dimethylaniline is similar to their neutralisation with quinoline (see Fig. 7). In these titrations also, the formation of the acid and the normal salts as reddish-yellow and light yellow solids is indicated. Both the normal salts have been isolated and analysed.[1]

These neutralisation reactions, in which the relatively undissociated molecules of acetyl chloride are formed, are similar to those in water or other polar solvents.

EXPERIMENTAL

Acetyl chloride was purified as already described,[8] and the fraction with a take off ratio of 1 : 10 was collected. Acids and bases were purified by fractional distillation, and quaternary ammonium chlorides were crystallised from lime-dried alcohol.

The solutions of acids and bases in acetyl chloride were prepared in a dry box and the transfer of solutions was carried out by using compressed dry nitrogen. A glass conductivity cell, with replaceable platinum electrodes in ground-glass joints and equipped with a micro-burette and calcium chloride guard tube, was employed. The resistance of solutions was measured at 30° ± 0·1° by using a precision measuring bridge type WBR No. 108 with logarithmic indicator amplifier type, TAV,IKc, No. 034 (Wissenschaftlich-Technische Werkstatten, Wielheim/Oby., Germany).

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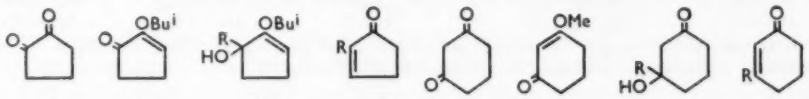
59. *Reduced Cyclic Compounds. Part VII.* A New Route to 2-Substituted* cyclo*Pent-2-enones.*

By M. F. Ansell and J. W. Ducker.

A convenient and unambiguous route to 2-substituted *cyclo*pent-2-enones by way of 2-*iso*butoxy*cyclo*pent-2-enone is described, with ten examples.

In connexion with other investigations [1]* we required a convenient and unambiguous method for the preparation of 2-substituted *cyclo*pent-2-enones (IV). The reported general routes are: (*a*) from the 1-substituted *cyclo*pentene *via* the nitroso-chloride (for IV, R = Me,[2] Pr^i,[3] *n*-pentyl,[2] and Ph [4]); (*b*) cyclisation of alkenoic acids (or the lactones of the related hydroxy-acids) or alkenoyl chlorides (for IV, R = Me,[1] Et,[1] Pr^n,[1] Pr^i,[1] Bu^n,[5,6] *n*-pentyl,[7] and *n*-hexyl [7–9]); (*c*) dehydrohalogenation of 2-substituted 2-halogeno*cyclo*pentanones (for IV, R = Me,[10] Et,[1] and Ph,[4,11]); and (*d*) from *cyclo*pentane-1 : 2-dione by treatment with a Grignard reagent followed by dehydration (for IV, R = Me [12]). The cyclisation and concomitant hydration of suitably constituted dienynes [13] or the cyclisation of dicarbonyl compounds [14] has been used as a route to *cyclo*pent-2-enones substituted in the 2- and other positions. 2-Phenyl*cyclo*pent-2-enone has been prepared [15] from 3-oxo-2-phenyl*cyclo*pentane-1-carboxylic acid by treatment with polyphosphoric acid, and the same reagent converts 2-*iso*propylidene*cyclo*pentanone into 2-*iso*propyl*cyclo*pent-2-enone.[1]

Of the available methods for the preparation of 2-substituted *cyclo*pent-2-enones, (*a*) is somewhat indirect and has been described [16] as being of little practical importance; (*b*) is ambiguous, as it can also give rise to 2-substituted *cyclo*hex-2-enones [1,9] and 2-substituted *cyclo*pent-4-enones; [7,9] and (*c*) involves preferential halogenation in the preparation of the starting material. Method (*d*) uses a readily available, although somewhat unstable, starting material and a molar excess of the Grignard reagent, but does constituted a convenient and unambiguous synthesis. We considered that the method could be further improved, by analogy with the route (V—VIII) devised by Born, Pappo,



(I) (II) (III) (IV) (V) (VI) (VII) (VIII)

and Szmuszkovic [17] for the preparation of 3-substituted *cyclo*hex-2-enones. We have therefore prepared 2-*iso*butoxy*cyclo*pent-2-enone (II), a stable liquid, from *cyclo*pentane-1 : 2-

* Part VI, *J.*, 1958, 3956.

[1] Ansell and Brown, *J.*, 1958, 2955.
[2] Rinkes, *Rec. Trav. chim.*, 1938, **57**, 176.
[3] Meerwein, *Annalen*, 1914, **405**, 129.
[4] Amiel, Löffler, and Ginsburg, *J. Amer. Chem. Soc.*, 1954, **76**, 3625.
[5] Dominquez, Diaz, and Slim, *Ciencia*, 1956, **16**, 151.
[6] Isikawa, Sakurai, and Someno, *Sci. Reports Tokyo Bunrika Daigaku*, 1940, **3**, *A*, No. 74, 293; *Chem. Abs.*, 1941, **35**, 8206.
[7] Plattner and St. Pfau, *Helv. Chim. Acta*, 1937, **20**, 1474.
[8] Maschmeijer, F.P. 765,515.
[9] Frank, Armstrong, Kwiatek, and Price, *J. Amer. Chem. Soc.*, 1948, **70**, 1379.
[10] Nazarov, Bergelson, Torgov, and Ananchenko, *Bull. Acad. Sci. U.S.S.R.*, 1953, 787.
[11] Winternitz, Mousseron, and Rouzier, *Bull. Soc. chim. France*, 1954, 316.
[12] Inhoffen and Krämer, *Chem. Ber.*, 1954, **87**, 488.
[13] *Inter al.*, Nazarov and Bakhmutskaya, *Zhur. obschei Khim.*, 1948, **18**, 1077.
[14] Hunsdiecker, *Ber.*, 1942, **75**, 455.
[15] Baker and Jones, *J.*, 1951, 787.
[16] Raphael in "Chemistry of Carbon Compounds," ed. E. H. Rodd, Elsevier, Amsterdam, 1950, Vol. IIa, p. 96.
[17] Born, Pappo, and Szmuszkovic, *J.*, 1953, 1779.

dione (I) by treatment of the latter with *iso*butyl alcohol in the presence of toluene-*p*-sulphonic acid. The former (II) reacts readily with a Grignard reagent to yield compound (III) which on treatment with dilute acid undergoes hydrolysis and dehydration to yield the 2-substituted *cyclo*pent-2-enone (IV). The use of strong acid at this stage causes polymerisation (cf. ref. 9). The validity of this method depends on the exclusive formation of an endocyclic double bond on dehydration of the intermediate hydroxy-ketone. That this should be so is supported by the observation [1] that 2-*iso*propylidene*cyclo*pentanone isomerises to 2-*iso*propyl*cyclo*pent-2-enone in the presence of acid, which is in keeping with the greater stability of an endo- than of an exo-cyclic double bond in a five-membered ring.[18]

We have applied this method to the preparation of two new and eight known 2-substituted *cyclo*pent-2-enones (see Table). The constants we obtained agree with the

2-*Substituted* cyclo*Pent-2-enones* (IV). (*Previous constants are in parentheses.*)

No.	2-Subst. R	B. p./mm.	n_D *	M. p. of 2 : 4-dinitrophenylhydrazone	M. p. of semicarbazone
1 [1]	Me	48—50°/14 (51—52°/13)	1·4744 (1·4798)	221—222° (221—222°) [b]	—[a]
2 [1]	Et	69—72°/16 (76—78°/23)	1·4728 (1·4747)	219—220 [c] (219—220)	209—210° [d] (196—198°)
3 [1]	Pr^n	85—86°/20 (90—91°/24)	1·4730 (1·4743)	198—199 [c] (177—178)	217—219 [c] (217—218)
4 [1]	Pr^i	88—90°/22 (84·5—85°/25)	1·4720 (1·4721)	— (202—203)	205—207 [f] (203—204)
5 [5,6]	Bu^n	98—100°/12 (95—102°/30; 102°/5)	1·4749 (1·4657,† 1·4759))	137—138 [f] (128—130·5, 177·4)	199—200 [c] (200—201, —)
6 [7]	*n*-Pentyl	114—116°/15 (108°/10)	1·4743 (1·473)	99—100 [f] (—)	200—201 [c] (199—200)
7 [5,8]	*n*-Hexyl	88—89°/1 (126—129°/30; 97—100°/5)	1·4744 (1·4729,† 1·4675)	88—89 [f] (92—93, —)	196—197 [c] (190—191, 194·5—196)
8 [15]	Ph	107—109°/1 (110—113°/2) [g]	— (—)	209—210 [c] (209—210)	235—236 [b] (235—237)
9	Ph·[CH$_2$]$_2$	97—98°/0·1	1·5490	153—154 [d]	254—256 [f]
10	Ph·[CH$_2$]$_3$	131—132°/0·1	1·5437	118—119 [c]	190—191

* At 20°, but † at 30°. [a] Oxime, m. p. 127—128° (lit.,[1] 127—128°). Tablets. Laths. [d] Prisms. [e] Needles. Plates. [g] M. p. 72—73° (lit.,[15] m. p. 72°).

No.‡		Found (%) C	H	N	Formula	Required (%) C	H	N
2	Ketone	76·3	9·2	—	$C_7H_{10}O$	76·3	9·2	—
2	SC	56·9	7·9	25·3	$C_8H_{13}ON_3$	57·5	7·8	25·1
3	Ketone	77·6	9·5	—	$C_8H_{12}O$	77·4	9·7	—
3	DNP	55·1	5·3	18·0	$C_{14}H_{16}O_4N_4$	55·3	5·3	18·4
5	Ketone	78·0	9·8	—	$C_9H_{14}O$	78·2	10·2	—
5	DNP	—	—	17·5	$C_{15}H_{18}O_4N_4$	—	—	17·6
5	SC	61·6	8·8	21·3	$C_{10}H_{17}ON_3$	61·5	8·8	21·5
6	DNP	—	—	16·9	$C_{16}H_{20}O_4N_4$	—	—	16·9
7	DNP	—	—	16·4	$C_{17}H_{22}O_4N_4$	—	—	16·2
7	SC	64·9	9·7	18·8	$C_{13}H_{21}ON_3$	64·5	9·5	18·8
9	Ketone	83·5	7·8	—	$C_{13}H_{14}O$	83·8	7·6	—
9	DNP	61·8	5·0	15·1	$C_{19}H_{18}O_4N_4$	62·3	5·0	15·3
9	SC	68·9	6·6	17·6	$C_{14}H_{17}ON_3$	69·1	7·0	17·3
9	Oxime § [e]	—	—	6·5	$C_{13}H_{15}ON$	—	—	7·0
10	Ketone	83·9	8·2	—	$C_{14}H_{16}O$	84·0	8·0	—
10	DNP	—	—	14·9	$C_{20}H_{20}O_4N_4$	—	—	14·7
10	SC	70·3	7·6	16·0	$C_{15}H_{19}ON_3$	70·0	7·4	16·3

‡ SC = Semicarbazone; DNP = 2 : 4-dinitrophenylhydrazone. § M. p. 81—82°.

recorded values when the *cyclo*pent-2-enones have been prepared by unambiguous methods, but discrepancies appear when the latter have previously been obtained by method (*b*).

[18] Turner and Garner, *J. Amer. Chem. Soc.*, 1958, **80**, 1424.

Experimental

2-iso*Butoxy*cyclo*pent-2-enone*.—A solution of *cyclo*pentane-1 : 2-dione [19] (22 g., 0·26 mole) and toluene-*p*-sulphonic acid (2 g.) in benzene (390 ml.) and *iso*butyl alcohol (96 ml.) was heated under reflux for 2 hr., the water formed in the reaction being removed by a Dean and Stark separator. The cold reaction mixture was washed with 5% sodium hydrogen carbonate solution, 5% sodium hydroxide solution and water, dried ($MgSO_4$), and distilled, to yield, after removal of the solvent, 2-iso*butoxy*cyclo*pent-2-enone* (26 g., 67%), b. p. 130—132°/15 mm., n_D^{20} 1·4770 (Found: C, 69·6; H, 8·8. $C_9H_{14}O_2$ requires C, 70·1; H, 9·1%).

2-*Substituted* cyclo*Pent-2-enones*.—2-*iso*Butoxy*cyclo*pent-2-enone (4 g., 0·025 mole) in ether (20 ml.) was added to a stirred solution of the required Grignard reagent (0·03 mol.) in ether (40 ml.) at such a rate that gently refluxing was maintained. After being stirred for 30 min. at room temperature the mixture was poured on ice and ammonium chloride, and 2N-hydrochloric acid added until two phases were obtained. The aqueous layer was separated and extracted with ether, and the combined ethereal solutions were washed with 5% aqueous sodium hydrogen carbonate and water, dried ($MgSO_4$), and distilled, to yield the 2-substituted *cyclo*pent-2-enone (45—75%). The 2 : 4-dinitrophenylhydrazones (orange to crimson) were crystallised from ethanol–chloroform, and the oximes and semicarbazones from ethanol.

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Mile End Road, London, E.1. [*Received, July 22nd*, 1958.]

[19] Dutch P. 58,279; *Chem. Abs.*, 1947, **41**, 4807.

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60. *Magnetochemistry. Part I. Introduction and Apparatus.*

By B. N. Figgis and R. S. Nyholm.

An apparatus is described for the measurement of the temperature-dependence of the magnetic susceptibility by the Gouy method from 80° to 500° K. The susceptibility of $CuSO_4,5H_2O$ from 90° to 300° K is reported.

In these two papers the magnetic susceptibilities of a number of co-ordination compounds of the transition series of elements are reported over the temperature range 80—400° K. This Part describes the equipment and indicates some general considerations which underlay the choice of compounds and the interpretation of the results.

The study of paramagnetic susceptibilities provides valuable information on the oxidation states of transition elements in co-ordination compounds. Also, if the number of unpaired electrons can be deduced from magnetic data it is often possible to infer the stereochemistry of the metal atom. Under certain conditions, even when the number of unpaired electrons is the same (*e.g.*, d^7 spin-paired Co^{II} complexes), two possible shapes can be distinguished by measuring the deviation from the spin-only moment. However, it has become increasingly apparent recently that care is necessary in interpreting magnetic data if obtained at room temperature only. Thus we now recognise that intra- or intermolecular antiferromagnetic interactions may not be uncommon in complex ions. Also, spectroscopic ground-state levels of transition-metal ions usually do not conform to the simplification that no energy-level separations $\sim kT$ from the lowest level occur. Such facts make it necessary to examine the magnetic properties in greater detail. These remarks apply particularly to the ions of the second and third transition series where antiferromagnetic interactions seem common and spin–orbit coupling is large. In a great many instances the information required for reliable deductions from magnetic data can be obtained by measuring the susceptibility over a range of temperature. In most cases the valuable information is to be obtained below room temperature and often it is sufficient to go down to the temperature of liquid air, 80° K.

The ideal paramagnetic substance obeys the Curie law $\chi \propto 1/T$, or rather, the closely associated Langevin–Debye expression $\chi_M = N(\mu^2/3kT + \alpha)$ where μ is the " magnetic moment " and α is the " temperature-independent paramagnetism " or " Van Vleck high-frequency term; " α is generally small compared with the term in μ, when this exists. Exchange interactions between neighbouring spins in a paramagnetic substance (ferromagnetism and antiferromagnetism) lead to departure from the Curie law, as also do electronic ground states in which energy separations $\sim kT$ appear. Ferromagnetism can be detected, in principle at least, by susceptibility measurements at varying field strengths, but this effect does not appear to be very common in co-ordination compounds, unless due to impurities. Antiferromagnetism results from antiparallel alignment of spins on neighbouring metal atoms; it causes a decrease in the susceptibility as compared with that expected for normal paramagnetism. At a sufficiently low temperature an antiferromagnetic compound shows a characteristic maximum in the susceptibility–temperature curve, at the Néel temperature. Above this temperature antiferromagnetism gives rise to a positive value of θ in the Curie–Weiss law equation $\chi_M \propto 1/(T + \theta)$; however, it is by no means the only cause of positive values of θ. These can also arise from the absence of a simple electronic ground state from the ion in question. It has often been the custom to calculate a quantity $\mu = 2{\cdot}84\sqrt{[\chi_M/(T + \theta)]}$ for a substance which follows the Curie–Weiss law, in place of the relationship obtained from the Langevin–Debye expression (α being ignored): $\mu = 2{\cdot}84\sqrt{(\chi_M T)}$. Strictly, this is unjustified unless it is known that a positive value of θ has its origin in an interaction of an antiferromagnetic nature; if this is not so it must be accepted that μ_{eff} is a function of temperature. We adopted the latter procedure.

The form of departure from the Curie law of temperature-dependence of the magnetic susceptibility arising from non-simple electronic ground states depends on the details of the ground state; this will be discussed along with the measurements on the group of compounds pertinent to the ion under consideration. In general, the lack of simplicity of the electronic ground state of an ion is associated with incomplete quenching of the orbital angular momentum of the ion by ligand fields and also with spin–orbit coupling. Since the former effect is a function of the stereochemical environment of the ion, information on the behaviour of the magnetic susceptibility with temperature with different stereochemical arrangements is desirable.

In the second and third transition series of ions magnetic data are scanty and it seems that the influences of antiferromagnetism, unusual stereochemistries, and large spin–orbit couplings make the interpretation of data at room temperature uncertain. One of our main purposes is to find out how reliable magnetic moment measurements are at room temperature in representing the magnetic properties of the system. Little is known from direct spectroscopy of the spin–orbit coupling constants to be used in connection with ions of elements of the second and third transition series; it is necessary to obtain a value for these constants from magnetic data on suitable systems to enable the properties of other systems to be accounted for.

Apparatus.—The use of the Gouy method for the measurements of magnetic susceptibilities, at temperatures other than that of the room, involves disadvantages, the chief of which is keeping the required temperature uniform and constant over a comparatively large volume. Almost equally important is the need to use a magnetic field of sufficient magnitude over an even larger volume. However, the conveniences it offers over other methods in dealing with a wide range of solid and liquid chemicals led us to adapt it to our temperature-dependence measurements, overcoming the disadvantages as completely as possible. In most previous temperature-dependence measurements by the Gouy method data are lacking concerning the uniformity of temperature over the whole specimen and its constancy during reasonably long periods. Often the methods employed cannot be expected to lead to high accuracy. Indeed, many temperatures quoted in the literature in this connection are probably in error by several degrees, particularly in the region of 150° K.

With our equipment the mean temperature of the specimen is controllable to within 0·1°

at any temperature within the range 80—500° K; the temperature gradient along the sample never exceeds 0·5° and is much less at the important low temperatures. The mean temperature can be measured to within 0·2° over the range. A magnetic field of up to 7500 oersteds is available at the lower end of the 10 cm. specimen, and is arranged to vanish at the other end of it. Gram-susceptibilities in the range 1—500 $\times 10^{-6}$ can be determined with an accuracy of about 0·5% in favourable circumstances and of about 2% in adverse ones.

As a check, the susceptibility of $CuSO_4.5H_2O$ was measured; this, for single crystals, has been reported several times.[2]

Description of the Apparatus.—(1) *Magnet and balance.* The magnetic field was derived from an electromagnet of the design described by Bates and Lloyd-Evans,[3] supplied with the required D.C. from a motor–generator. At an exciting current of 20 A, about 7500 oersteds was developed between the pole pieces 7·5 cm. apart and 8 cm. in diameter. The current could be decreased to a minimum of 2 A, giving then about 1400 oersteds. The current was controlled through external excitation of the generator, sometimes manually by rheostats in series with the generator field coils, and in other cases automatically through a servoamplifier system

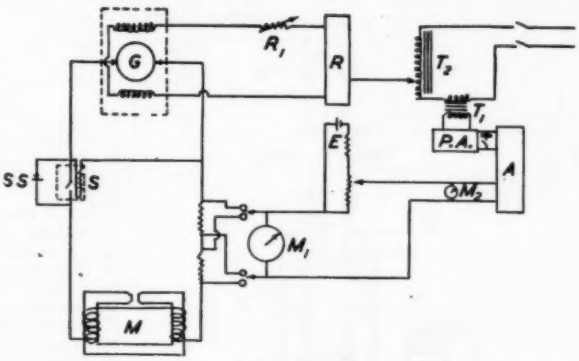

FIG. 1. *Magnet current supply circuit.*

M, Magnet. *G*, Generator. *S*, Sunvic 602 hot-wire switch. *SS*, Surge suppressor. M_1, Magnet current meter, 0—5, 0—25 amp. M_2, Error signal meter, 0—100 mv. *A*, D.C. amplifier. *P.A.*, Power amplifier, 20 w. *R*, Rectifier, to supply 100 v at 0·5 amp. *E*, 1·5 v. T_1, Output transformer, 10,000—100 ohms. T_2, "Variac" continuously variable autotransformer. R_1, 100 Ohm rheostat.

feeding the field coils. These circuits are shown in Fig. 1. Control was available to within the reading accuracy of the meter, *i.e.*, 0·05 A in the range 10—25 A, and 0·01 A in the range 2—5 A. At the highest currents magnetic-field control was to within 0·1% as saturation of the magnet core was approached. However, at lower currents the field depended more or less directly on the current and the field regulation could not then be made better than 0·5%. Thus the errors in the measurements of the susceptibilities arising from field control varied from 0·2 to 1%.

The magnet current was automatically regulated by balancing the potential drop across the current-measuring meter against a potential from a standard battery. The "out-of-balance" was fed as an error signal to a Brown model 351921 D.C. amplifier, followed by a 20 w power amplifier, which delivered a 50 volt A.C. voltage of suitable phase in series with the A.C. supply to the rectifier supplying the generator field coils to alter the magnet current to reduce the error signal. The current could thus be held at a given value as accurately as could be read on the meter, as indicated above.

The balance used for measuring the forces developed was a Sartorius model S.M.10 on which each scale division was 0·1 mg. and could be interpolated to 0·01 mg. The forces encountered in the work on paramagnetism in the transition-metal compounds could be measured with an accuracy rarely worse than 1% and mostly about 0·5% or better.

The relative susceptibilities so measured are accurate to within about 1% in general, although with small forces and small magnet currents, up to 2% error may be expected. Owing to the nature of the special long, completely filled Gouy tube required in conjunction with the cryostat, the accuracy of the absolute susceptibilities determined with it were not as good as usual in the Gouy method, as the packing of solids presents problems. However, the

[1] Figgis and Nyholm, *J.*, 1954, 12.

[2] Krishnan and Mookherji, *Phys. Rev.*, 1936, **50**, 860; 1938, **54**, 533, 841; Gorter and de Haas, *Comm. Kammerlingh Onnes Lab. Leiden*, 1930, No. 210d, 39.

[3] Bates and Lloyd-Evans, *Proc. Phys. Soc.*, 1933, **45**, *A*, 425.

susceptibilities were adjusted at room temperature to the value found at that temperature on a more conventional apparatus. Calibration of the Gouy tubes was performed with 31·31% w/w $NiCl_2$ (anhydrous) solution.[4]

(2) *Temperature control.* (a) *Cryostat.* This (Fig. 2) consists essentially of a chamber 1·5 cm. in diameter and 18 cm. in length in which the Pyrex glass Gouy tube (3 mm. internal diam. and 10 cm. long) is hung. This chamber is thermally insulated by a variable vacuum from a bath of liquid refrigerant (usually oxygen or nitrogen). A heating coil, spirally wound round the length of the chamber, and capable of dissipating 15 w, counterbalances the heat loss across the vacuum. A magnetic shield, consisting of a thick-walled iron tube 8 cm. long, encloses the upper end of the Gouy tube and makes the magnetic field at that point disappear. This substantially reduces the length of the Gouy tube required. A platinum wire wound

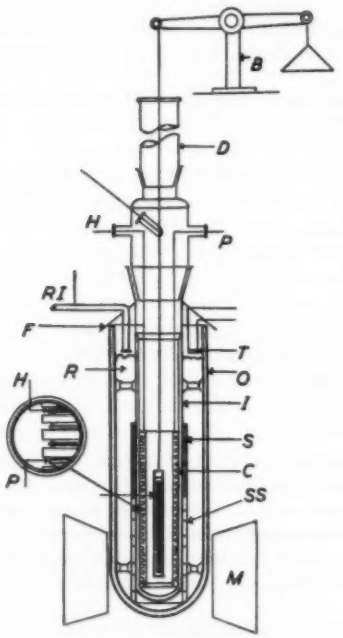

FIG. 2. *Cryostat.*

B, Balance.
C, Controlled block.
D, Draught shield.
F, Icing shield.
H, Heater.
I, Inner Dewar vessel.
M, Magnet pole.
O, Outer Dewar vessel.
P, Platinum resistance thermometer.
R, Refrigerant.
RI, Refrigerant inlet.
S, Magnetic shield.
SS, Magnetic shield support.
T, Thermistor.

between the spirals of the heating coil serves as a resistance thermometer for temperature control; its room-temperature resistance is about 10 ohms.

An Edwards " Speedivac " model 2S50 high-vacuum pump produced the vacuum in the inner Dewar flask, which was silvered. For operation *at*, and for about 40° *above*, the refrigerant temperature, air at atmospheric pressure was allowed to remain in the inner Dewar flask; for temperatures 40—100° *above* the refrigerant temperature the pressure in this vessel was kept at about 10^{-3} mm. by a suitable leak; from there to room temperature the best vacuum of the pump was employed (about 10^{-4} mm.). For operation above room temperature no refrigerant was used. A drying tube [$Mg(ClO_4)_2$] at the inlet to the Dewar vessel prevented moisture from condensing in it and attacking the silvering.

The refrigerant level was kept constant in the outer Dewar vessel by means of the device set out in Fig. 3. A thermistor, of room-temperature resistance 500 ohms, was held slightly above the desired refrigerant level and heated by a coil dissipating 1 w. A Sunvic model 602 high-vacuum switch was in series with the thermistor and the combination was excited with 60 v A.C. At room temperature sufficient current was passed by the thermistor to close the switch, which then operated a small compressor to force air into a 5 l. refrigerant storage vessel.

[4] Nettleton and Sugden, *Proc. Roy. Soc.*, 1939, *A*, **173**, 313.

Refrigerant was thus ejected into the outer Dewar vessel. When the refrigerant level had risen sufficiently to cool the thermistor, its increased resistance reduced the current and so switched off the compressor. A small leak dissipated the pressure in the storage vessel, and the ejection of refrigerant ceased.

The consumption of refrigerant depended upon the liquid chosen and the temperature of operation of the cryostat. For oxygen about 500 ml. were used per hour.

(b) *Temperature-control circuit.* The circuits for automatic control at any desired temperature are shown in Fig. 4. A platinum-resistance thermometer, comprising 12 feet of 32 s.w.g.

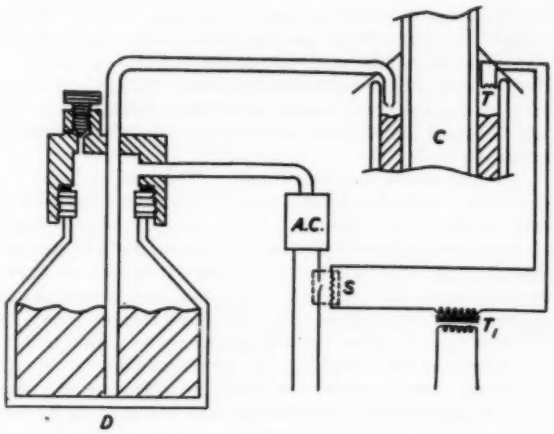

FIG. 3. *Constant refrigerant level mechanism.*

C, Cryostat.
D, 5 Litre storage Dewar vessel.
T, Theristmor.
T_1, Transformer, 240—60 v.
S, Sunvic 602 hot-wire switch.
A.C., Air compressor.
V, Air escape valve.

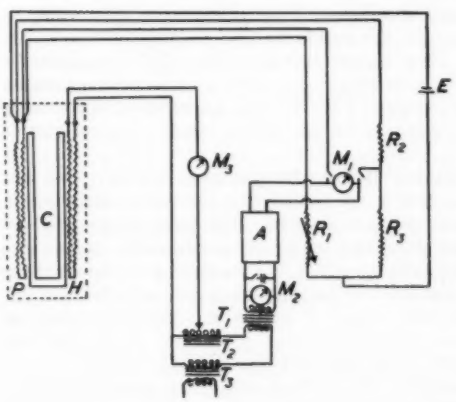

FIG. 4. *Temperature-control circuit.*

C, Cryostat. *P*, Platinum-resistance winding. *H*, Heater winding. R_1, 5 Decade resistance box. R_2, 10 Ohms. R_3, 300 Ohms. *E*, 6 v. M_1, Error-signal meter, 0—100 μv. M_2, Amplifier-output meter, 0—200 v, A.C. M_3, Heater-current meter, 0—1 amp. A.C. *A*, D.C. amplifier. T_1, Output transformer, 5000—15 ohms. T_2, "Variac" continuously variable autotransformer. T_3, Transformer, 240—17 v.

platinum wire, was wound on the outside of the controlled copper-block chamber, between the windings of the heating coil. The insulation from the block for the thermometer and the heating coil was a layer of 0·07 mm. thick "Teflon" foil. No particular care to avoid strain in the wire was exercised in winding the platinum as this thermometer was not used as a primary standard. The ends of the thermometer were taken to mica-insulated terminal posts on the upper end of the block. From these points current and potential leads were taken to the binding posts at the top of the cryostat. All connections at the terminals at the block and to the ends of the heating coil were silver-soldered. The leads from the block terminals to the top binding posts were spiralled inside the wall of the inner Dewar vessel to reduce heat transfer along them.

The resistance thermometer formed one arm of a Wheatstone bridge, whose other, variable, arm was a 5 decade resistance box of maximum resistance 1111·1 ohms. This bridge was

excited by 6 v D.C. The " out-of-balance " of the bridge was amplified by means of a Leeds and Northrop model R-820-1 D.C. amplifier which delivered about 150 v A.C. at 7 w to an output transformer of 15 ohms output impedance. The secondary winding of this transformer was in series with the primary of a continuously variable auto-transformer; this arrangement was fed from 17 v A.C. The output of the variable transformer was the supply for the heating coil of the cryostat. The phase of the voltage supplied by the output transformer was determined by the sign of the out-of-balance signal to the amplifier. According as this voltage was in or out of phase with the 17 v A.C. supply, it increased or decreased the power supplied to the heating coil. The phase relationship was arranged so that the change of heater power was in the direction required to reduce the error signal. Meters for reading the error signal, the amplifier output voltage, and the heater current were provided.

Operation of the temperature control was as follows. With the amplifier output voltage short-circuited by a condenser, the heater current was adjusted to maintain the required temperature with a suitable vacuum in the inner Dewar flask. The Wheatstone bridge was balanced, and the short circuit removed from the amplifier output; the temperature was then controlled at the required value.

(c) *Measurement of temperature.* The temperatures of the specimen were measured with a nichrome–constantan thermocouple so inserted that its " hot " junction was beside the midpoint of the Gouy tube, with this tube in position. When temperature equilibrium had been attained the thermocouple was withdrawn, and the susceptibility immediately measured. The thermocouple was calibrated against a platinum-resistance thermometer (not to be confused with the one in the cryostat), which had a resistance of about 2 ohms at 20° c. The resistance thermometer was calibrated at the liquid-oxygen point, the ice point, and the steam point; a check at the CO_2 point showed agreement to within 0·05°. The resistance of the thermometer was measured by comparing the potential drop across it, measured on a Leeds and Northrop model K2 potentiometer, with that developed across a standard 1 ohm resistance in series with it. The thermometer calibration was accurate to 0·1° or better over the range 80—500° K. The nichrome–constantan thermocouple was calibrated against this resistance thermometer by enclosing both in a 4 kg. brass block contained in a Dewar flask. Readings were taken at approximately 5° intervals. This close calibration was necessary because this thermocouple, in common with all similar combinations, may show a discontinuity in the E.M.F.–temperature curve. In this case, the discontinuity was of about 50 μv at −140° c. Use of the thermocouple within a few degrees of this point was avoided. The calibration of the thermocouple was accurate to 0·2° throughout the range. The E.M.F. of the thermocouple was measured on the same potentiometer as above.

Performance of the Apparatus.—With a suitable vacuum for the inner Dewar vessel any temperature from the b. p. of the refrigerant to 500° K can be attained and kept indefinitely to within 0·1° with the centre of the Gouy tube as measuring point. The temperature gradient between the ends of the Gouy tube was investigated at various temperatures by means of a differential thermocouple with a junction at each of the ends. The gradient was absent at the refrigerant temperature and rose more or less regularly with rising temperature to 0·5° per cm. at room temperature; the rise continued above this to about 1° at 400° K. With no refrigerant in the outer Dewar flask the gradient at room temperature was, of course, absent and rose steadily to about 0·5° over the length (10 cm.) of the specimen for operation at 500° K.

Thermal equilibrium of the controlled chambers is reached about 15 min. after attaining a required temperature. However, much longer was required for equilibrium to be reached with respect to the forces exerted on a specimen at a particular temperature. The period necessary for constancy of the force on the specimen varied with temperature; for all but the lowest temperatures 1 hr. was sufficient; near the refrigerant temperature about 2 hr. were required. In the course of the measurements on $CuSO_4,5H_2O$ the numerical reproducibility of the apparatus was checked under the most favourable conditions of operation, *i.e.*, high magnet current and high forces; the force on a given sample at a given temperature could be reproduced to within 0·5%. This agrees with the estimates for this accuracy made from the performance of the current regulator and the balance sensitivity.

Calibration of Gouy Tube.—The calibration of the Gouy tube in temperature-dependence measurements presents difficulty in the assignment of the constants α and β in the usual formula, $10^6\chi = [\alpha + \beta(F + \delta)]/w$, where α allows for the medium (usually air) occupying the tube subsequently displaced by the specimen; β is dependent only on the geometry of the tube and

the magnetic field; δ is the force exerted on the tube alone, and F that on the tube + specimen; w is the weight of the specimen.

Whereas β is essentially independent of temperature, α and δ are likely to be functions of it. It is possible to eliminate the correction α by performing measurements in an atmosphere of nitrogen, and this was the usual procedure. The specimen chamber was evacuated and dry nitrogen admitted. A very slow flow of nitrogen was maintained across the top of the cryostat where it joins the draught shield. This prevented the diffusion of air into the specimen chamber and did not affect the operation of the balance. The correction δ was found by measuring the

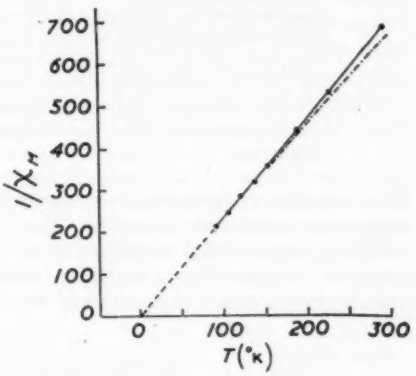

FIG. 5. *Variation of the inverse of the corrected molar susceptibility of a powdered* $CuSO_4.5H_2O$ *specimen with temperature.*

———— Experimental curve, χ_M
– – – – – ,, ,, χ'_M
– – – – – – – Low-temperature extrapolation of χ_M

force developed on the Gouy tube in the nitrogen atmosphere over the temperature range. For a typical tube δ decreased from 2·0 mg. at 350° K to 1·0 mg. at 90° K, apparently owing to the paramagnetic impurities in the (diamagnetic) glass.

The Susceptibility of Copper Sulphate Pentahydrate.—In order to check the operation of the apparatus the susceptibility of powdered $CuSO_4.5H_2O$ was measured from 90° to 300° K. This substance has an anisotropic susceptibility which obeys a Curie–Weiss law with a Weiss temperature of about 0·7°, as the mean for the three principal susceptibilities, and a mean Curie constant of 0·457.[2] The inverse of the molar susceptibility for our powdered specimen, corrected for the diamagnetic constitution, is plotted against temperature in Fig. 5. The broken line indicates the extrapolation to absolute zero, and also the course of the curve if no correction for the diamagnetic constituents is made. It is straight, within experimental error. The correction for diamagnetic constituents was 74×10^{-6}/mole. With a large Gouy tube the mass susceptibility is found to be $6{\cdot}05 \times 10^{-6}$ c.g.s. units. This is considered to be correct to better than 1½%. It agrees well with the most reliable values in the literature, namely those of Sugden [5] and of Gorter and de Haas [2] who report $6{\cdot}14 \times 10^{-6}$ and $5{\cdot}95 \times 10^{-6}$ c.g.s. units, respectively.

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[5] Sugden, *J.*, 1932, 161.

61. *Magnetochemistry. Part II.* The Temperature-dependence of the Magnetic Susceptibility of Bivalent Cobalt Compounds.*

By B. N. Figgis and R. S. Nyholm.

The magnetic susceptibilities of a number of quadri- and sexa-covalent cobalt(II) complexes from 80° to 300° K are reported. The size of the orbital contribution to the magnetic moment is determined and is correlated with the co-ordination number and stereochemistry. Values of the Weiss constant (θ) are small and the moments in the range 1·9—2·0 B.M. and 2·1—2·9 B.M. for the octahedral and square spin-paired complexes respectively are sensibly the same over the temperature range studied. The significance of the moments of spin-free octahedral and tetrahedral complexes is also discussed.

The correlations between stereochemistry and orbital contribution to the magnetic moment in compounds of bivalent cobalt [1] are summarised in Table 1. The existence of a relatively large orbital contribution to the moment in octahedrally co-ordinated compounds of the spin-free (or so-called " ionic ") type, and of a smaller contribution in tetrahedrally co-ordinated compounds of the same type, is paralled in a modified form by the

Table 1. *Electronic configurations of various cobaltous complexes.*

Type of complex	Co-ordination no. and stereochemistry	Electronic configuration	Unpaired electrons
Spin-free	Quadricovalent tetrahedral	$3d$ ($d\gamma$ $d\varepsilon$) $4s$ $4p$	3
	Sexacovalent octahedral	$3d$ ($d\varepsilon$ $d\gamma$) $4s$ $4p$ $4d$	3
Spin-paired	Quadricovalent square planar †	$3d$ (1 2 3 4) $4s$ $4p$ 1. d_{z^2} 2. d_{yz}, 3. d_{xz} 4. d_{xy}	1
	Sexacovalent (presumably tetragonal) (*a*)	$3d$ ($d\varepsilon$ $d\gamma$) $4s$ $4p$ $4d$	1
	Sexacovalent (presumably tetragonal) (*b*) *	$3d$ ($d\varepsilon$ $d\gamma$) $4s$ $4p$ $5s$	1

The symbol [••] indicates the bonding orbitals (if used).
* Originally proposed [1] but now considered improbable.
† From Fig. 1; see also ref. 22.

behaviour of compounds of the spin-paired (or so-called " covalent " type). In the latter type, however, it was found that, although sexacovalent complexes were characterised by the virtual absence of orbital contribution, yet in the square co-ordinated compounds this may have an appreciable value. To our previous list,[1] on which we based the association of stereochemistry with orbital contribution for the spin-paired compounds, may be added

* Part I, preceding paper.

[1] Figgis and Nyholm, *J.*, 1954, 12.

the following measurements which support the previous proposals. The moment of the complex of bivalent cobalt with the sexadentate ligand

$$HO{\cdot}C_6H_4{\cdot}CH{:}N{\cdot}[CH_2]_2{\cdot}S{\cdot}[CH_2]_2{\cdot}S{\cdot}[CH_2]_2{\cdot}N{:}CH{\cdot}C_6H_4{\cdot}OH$$

is 1·82 B.M.[2] Two compounds of the quadricovalent type, $[Co(o\text{-aminobenzenethiol})_2]^0$, *i.e.*, $[Co(NH_2{\cdot}C_6H_4{\cdot}S)_2]^0$, and $[Co(ethylthiopropanethiol)_2]^0$, *i.e.*, $[Co(CH_3{\cdot}CH_2{\cdot}S{\cdot}[CH_2]_3{\cdot}S)_2]^0$, have been reported to have moments of 2·7 and 2·5 B.M. respectively.[3]

Most previous magnetic measurements on cobalt(II) complexes were for one temperature only and the interpretation of values of μ_{eff} calculated them was uncertain. Our measurements were undertaken to obtain results as to the separation between possible energy levels (relative to kT) and information concerning the ground states of the various types of cobaltous compound. In particular it was desired to establish (i) that the large orbital contribution occurring in the octahedral *weak field* and the square-planar *strong field* cases are " genuine " in so far as they are maintained over a range of temperature; (ii) to find whether the simple ground states suggested by the close to spin-only value moments are confirmed by simple magnetic behaviour with regard to temperature.

The orbital contribution of spin-free cobaltous compounds arises as follows. The ground term of the Co^{2+} ion, d^7, is ^4F; there are three unpaired electrons and the ion is seven-fold degenerate with respect to electric fields. An octahedral arrangement of ligand atoms about the central cobalt ion gives rise to a crystalline field of cubic symmetry which splits the seven levels of the F state into two orbital triplet sets and a singlet one, with separations between those of the order of 20,000 cm.$^{-1}$. One of the triplets, predominantly $d_\epsilon^5 d_\gamma^2$, lies lowest. The orbital angular momentum of the ion results from orbital degeneracy, or near degeneracy if fields of less than cubic symmetry are present, within this triplet.[4] For this d^7 three-spin system the magnetic moments should lie somewhere between the limits $\mu_{eff} = \sqrt{[4S(S+1)]} = 3{\cdot}88$ B.M. and $\mu_{eff} = \sqrt{[4S(S+1) + L(L+1)]} = 5{\cdot}2$ B.M., where S is the total spin angular momentum of $(3/2)\hbar/2\pi$ and L is the total orbital angular momentum of $3\hbar/2\pi$. The actual value depends upon the amount of L remaining associated with the ground-state orbital triplet. On the other hand, when the ligand arrangement about the cobalt atom is tetrahedral there is again a cubic field set up, but it is now of opposite sign to that of the octahedral case so that in these circumstances the ground orbital state is the singlet. As there is no orbital angular moment associated with the singlet level the moment for the system is expected to lie close to the spin-only value.

In fact some orbital contribution occurs in the tetrahedral complexes, for experimental moments mostly lie in the range 3·9—4·4 B.M. This orbital contribution is considered to arise from the mixing of some of the next higher orbital triplet level into the singlet by the operation of spin–orbit coupling; the spin-only moment is multiplied by a factor $(1 + 4A/3\Delta)$. The value of Δ is probably about 5000 cm.$^{-1}$ for tetrahedral complexes and A is the *single* electron spin-orbit coupling constant, 540 cm.$^{-1}$. Then μ_{eff} is expected to be ~4·5 B.M. The theory of the spin-paired case is not well developed. The unpaired electron of the spin-paired hexaco-ordinated cobalt(II) compounds may be accommodated either in the d_γ orbitals or, less likely, " promoted " to a 5*s* orbital. Although we originally favoured the latter we now consider this improbable (see Table 1). In either case, however, the magnetic properties of the system should be simple and devoid of orbital contribution since neither a $3d_z^2$ nor a 5*s* electron should give rise to orbital magnetism.

The effect of a strong tetragonal field on the magnetic properties of the *d* orbitals has not been considered in detail: it seems that the splittings will be as shown in Fig. 1. In a strong tetragonal field the concept of d_ϵ and d_γ orbitals loses much of its significance. If the field arises from four ligand atoms, regarded as point charges, placed at a distance a

[2] Dwyer, Gill, Gyarfas, and Lyons, *J. Amer. Chem. Soc.*, 1957, **79**, 1269.
[3] Livingstone, *J.*, 1957, 143.
[4] Abragam and Pryce, *Proc. Roy. Soc.*, 1951, *A*, **206**, 173.

from the central metal atom and on the x and y axes of the Cartesian system, the positions of the energies of the orbitals, relative to the centre of gravity, are:

$$d_z^2 \text{ at } -\left(\frac{6}{a^3}\overline{r^2} - \frac{9}{2a^5}\overline{r^4}\right)\frac{2Z}{105}; \qquad d_{xz} \text{ and } d_{yz} \text{ at } -\left(\frac{3}{a^3}\overline{r^2} + \frac{3}{a^5}\overline{r^4}\right)\frac{2Z}{105}$$

$$d_{xy} \text{ at } \left(\frac{6}{a^3}\overline{r^2} - \frac{8}{a^5}\overline{r^4}\right)\frac{2Z}{105}; \qquad d_{x^2-y^2} \text{ at } \left(\frac{6}{a^3}\overline{r^2} + \frac{19}{2a^5}\overline{r^4}\right)\frac{2Z}{105}$$

where Z is the charge assumed on the ligand atom and r is the radius from the central ion. We may compare these splittings with the d_ϵ–d_γ separation for the octahedral case which differs from the tetragonal case by the placing of two additional charges in the octahedral positions: [5]

$$d_\epsilon \text{ at } -\frac{4}{a^5}\overline{r^4}\cdot\frac{2Z}{21}; \qquad d_\gamma \text{ at } \frac{6}{a^5}\overline{r^4}\cdot\frac{2Z}{21}$$

In Fig. 1 are the separations for the square planar arrangement and for a metal ion–ligand atom separation of about 3 Å. An exact comparison of the separations with the d_ϵ–d_γ separation would require a knowledge of the values of $\overline{r^2}$ and $\overline{r^4}$ for the Co^{2+} ion but,

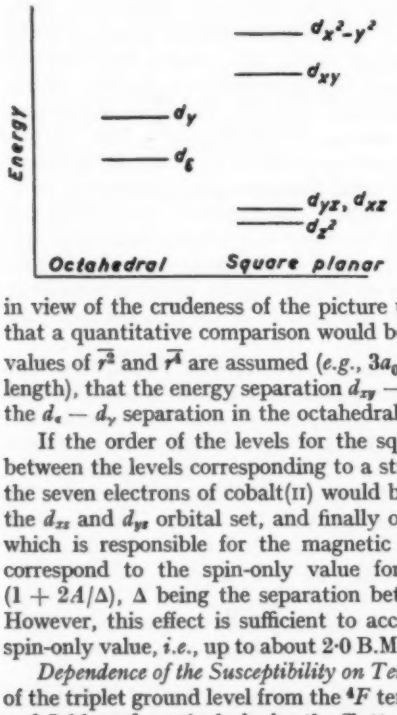

FIG. 1. *The splittings of the d orbitals in the field of four charges in a plane* $(\pm a, 0, 0), (0, \pm a, 0)$; $a = 3$ Å, $\overline{r^2} = 3a_0^2$, $\overline{r^4} = 30a_0^4$.

The d_ϵ and d_γ levels are given for the same conditions with charges in octahedral positions.

in view of the crudeness of the picture upon which the calculations are based, it is likely that a quantitative comparison would be of little value. It seems probable, if reasonable values of $\overline{r^2}$ and $\overline{r^4}$ are assumed (*e.g.*, $3a_0^2$ and $30a_0^4$, respectively; a_0 is the atomic unit of length), that the energy separation $d_{xy} - d_{x^2-y^2}$ in the square planar case is of the order of the $d_\epsilon - d_\gamma$ separation in the octahedral case.

If the order of the levels for the square planar case is as in Fig. 1 with separations between the levels corresponding to a strong field, *i.e.*, sufficient to force spin pairing, then the seven electrons of cobalt(II) would be distributed as follows: 2 in the d_{z^2} orbital, 4 in the d_{xz} and d_{yz} orbital set, and finally one in the d_{xy} orbital, and it is the last one alone which is responsible for the magnetic properties of the system. The moment should correspond to the spin-only value for one unpaired spin multiplied by a factor $\sim (1 + 2A/\Delta)$, Δ being the separation between the d_{xy} orbital and its neighbouring levels. However, this effect is sufficient to account for moments of only about 10% above the spin-only value, *i.e.*, up to about 2·0 B.M.

Dependence of the Susceptibility on Temperature.—The theory of the magnetic behaviour of the triplet ground level from the ^4F term of Co^{2+} has been developed in detail by Penney and Schlapp,[6] particularly for the Tutton salts, *e.g.*, $(NH_4)_2Co(SO_4)_2,6H_2O$, assuming that fields of predominantly cubic symmetry but with rhombic components were operative. However, as those authors did not have adequate data on the crystal structures, agreement between experiment and the theory, while encouraging, was not close. Owing to

[5] Bethe, *Ann. Physik*, 1929, **3**, 133.
[6] Penney and Schlapp, *Phys. Rev.*, 1932, **41**, 242, 666.

the fact that the ground level considered was the orbital triplet the treatment was difficult. They were able to account approximately for the room-temperature moment of 5·2 B.M., its decrease to 4·4 B.M. at 80° K, and the magnetic anistropy. The theory of the magnetic properties of the tetrahedrally co-ordinated type of cobaltous compound has not been given in such detail although Bose [7] dealt with it to some extent. It appears that the singlet ground state which is involved should be subject to no obvious effects which disturb the expected simple magnetic behaviour; there seems to be no reason for expecting departures from Curie's law. However, in view of the small orbital contributions which do occur some interest arises as to whether these are accompanied by deviations from Curie's law.

As far as the spin-paired or strong-field case is concerned no theoretical treatment of the temperature-dependence of the susceptibility has been attempted; the most that can be said is that the approximation of the octahedral type of compounds to the spin-only value of the moment at room temperature is very likely to be an indication of magnetic simplicity which should be paralleled by conformity with a Curie law. On the other hand, the lack of magnetic simplicity shown by the very appreciable orbital contribution in the square-planar compounds is likely to be reflected in a somewhat more complicated magnetic behaviour with temperature.

Published experimental data on the temperature-dependence of the magnetic susceptibility of cobaltous compounds are not extensive and are confined almost entirely to the spin-free or weak-field case. The Tutton salts $(NH_4, K, Rb)_2Co(SO_4)_2,6H_2O$ as well as $CoSO_4,7H_2O$ were studied in terms of the magnetic anisotropy by Jackson,[8] but at only three temperatures between 15° and 300° K, and doubt has been cast on the reliability of these results.[9] The same Tutton salts, together with Cs_2CoCl_4 and $CoBeF_4,7H_2O$, were studied by Bose,[7] and Guha [10] deal with $CoSO_4,7H_2O$ and $CoSeO_4,7H_2O$. These measurements also were primarily concerned with the anisotropy of the magnetic susceptibility. Amonst the spin-paired compounds Calvin and others [11] studied the susceptibility of the square compounds Co(ethylenediaminebis-salicylaldehyde) in both "active" and "inactive" forms and also the 3-methoxy- and the pyridine derivative of this compound. The rather extraordinary magnetic behaviour of the first two of these compounds, combined with the difficulty of being sure of their actual chemical identity, renders the significance of the measurements doubtful. The last of these compounds may have involved a quinquecovalent stereochemistry for the cobalt atom.

The values of θ reported in connection with the above measurements on the spin-free octahedral compounds vary from 15° to 30°; such values are as might have been expected for such a system. The only available result for the tetrahedral arrangement is 7° for θ for the compound Cs_2CoCl_4; this is distinctly lower than those for the octahedral case but not the vanishingly small value that a perfectly simple ground state requires: it is rather in line with the small amount of orbital contribution exhibited. For the spin-paired type of compound data are available only for the square-planar case, where θ values from −20° to 60° are reported; but little of significance can be deduced from this since the nature of the compounds concerned and the precision of the magnetic measurements are not well established.

Discussion.—The compounds studied are listed in Table 2.

(a) *Octahedral spin-free.* In common with all the Tutton salts, $(NH_4)_2Co(SO_4)_2,6H_2O$ crystallises with an octahedron of water molecules, slightly distorted by elongation in one axis, about the central cobalt atom.[12,13] The distortion of the octahedron must result in

[7] Bose, Thesis, Dacca University, 1946.
[8] Jackson, *Phil. Trans.*, 1923, **224**, 1.
[9] Banjeri, Chakrovooty, and Krishnan, *Phil. Trans.*, 1933, **232**, 99.
[10] Guha, *Proc. Roy. Soc.*, 1951, *A*, **206**, 353.
[11] Barkelew and Calvin, *J. Amer. Chem. Soc.*, 1946, **68**, 2257.
[12] Hoffmann, *Z. Krist.*, 1930, **75**, 158; 1931, **78**, 279.
[13] Halla and Mehl, *Z. anorg. Chem.*, 1931, **199**, 379.

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TABLE 2. *Diamagnetic corrections, magnetic moments at* 300° *and* 90° K, θ *values, and accuracies of the measurements of the relative susceptibilities at different temperatures for the compounds of bivalent cobalt studied.*

Stereochemistry and type		Diam. Corr. $\times 10^6$	μ_{eff} 90° K	μ_{eff} 300° K	θ (°)	Accuracy (%)
Octahedral, 3 unpaired electrons	$(NH_4)_2Co(SO_4)_2,6H_2O$	184	4·53	4·90	27	0·5
	Co(*o*-phen)$_3$(ClO$_4$)$_2$ [a]	394	5·54	4·70	11	0·5
	KCo(acetylacetone)$_3$	192	5·02	4·70	−15	2
Tetrahedral, 3 unpaired electrons	$HgCo(CNS)_4$	137	4·18	4·33	10	0·5
	Co(Ph·NH$_2$)$_3$Cl$_2$	167	3·96	4·19	27	1
Octahedral, 1 unpaired electron	$K_2BaCo(NO_2)_6$	147	1·73	1·88	25	1
	$K_2PbCo(NO_2)_6$	150	1·74	1·81	5	1
Square-planar, 1 unpaired electron	CoD$_3$(ClO$_4$)$_2$ [b]	454	1·98	2·10	10	0·5
	Co(phthalocyanine)	290	2·22	2·72	(60) [c]	1
	Co(en.sal.) [d]	151	2·06	2·24	25	1
	Co(E.T.T.) [e]	184	2·38	2·54	17	0·5

[a] *o*-Phen = *o*-phenanthroline. [b] D = *o*-Phenylenebisdimethylarsine. [c] It is not really justified to evaluate a θ in this case. [d] en.sal. = ethylenedi-iminebis-salicylaldehyde. [e] E.T.T. = ethylthiopropanethiol.

a tetragonal field of some magnitude, but this does not affect the essential arguments concerning the contribution of an orbital term to the moment by the triplet-type ground state. There is *X*-ray [14] evidence that the cobalt atom in [Co(*o*-phenanthroline)$_3$](ClO$_4$)$_2$ is octahedrally co-ordinated. Although one would confidently expect an octahedral stereochemistry for the cobalt in K[Co(acetylacetone)$_3$], some slight deviations from perfect symmetry in the crystal are probable because the ground state is only approximately $d_\epsilon^5 d_\gamma^2$, the ions outside the co-ordination sphere influence packing of the lattice, and the ligand is bidentate. Table 2 shows that the values of θ for these compounds of the octahedral weak-field type are 27°, 11°, and −15°. The 27° for $(NH_4)_2Co(SO_4)_2,6H_2O$ agrees quite well with the value of 22° reported by Jackson, considering that his value was obtained by averaging the results of anisotropy measurements. Such values of θ are of the same order as those in the literature; they show that, although the system is not magnetically simple, the deviations are not sufficiently large seriously to affect the moments concerned at any temperature studied. The orbital contribution involved is maintained substantially unchanged by temperature variation over the range of measurement.

(b) *Tetrahedral spin-free.* $HgCo(CNS)_4$ is known from *X*-ray evidence [15] to be formed by the sulphur atoms of each (CNS) group surrounding the cobalt atom tetrahedrally, the nitrogen atoms of that group being attached to four different mercury atoms which are also thus tetrahedrally co-ordinated. For this tetrahedral weak-field case the situation is not quite as much in conformity with expectations: in addition to Bose's value of 7° for Cs_2CoCl_4, we find values of 10° and 27° for θ pertaining to the compounds of the group. Values of θ as large as this are not to be associated with a ground state as simple as described above. Of course, θ values of this magnitude do not significantly affect the moments involved over the temperature range concerned, and the orbital contribution to the moment is clearly quite small. However, the lack of magnetic simplicity indicated is sufficient to warn us against taking too seriously the resemblance between the orbitally single ground state arising from the splitting of an *F* state and an *S* state.

(c) *Sexacovalent spin-paired.* A regular octahedral co-ordination of nitrite groups around the central cobalt atom in the cobaltonitrites has been reported by Ferrari and others [16] from *X*-ray studies. This is rather unexpected since, if the single unpaired *d* electron is in a d_γ (presumably d_{z^2}) orbital, a *lengthening* along one axis (*z*) of the octahedron is expected. It is unfortunate that other compounds of the octahedral strong

[14] Harris and Stevenson, unpublished work.
[15] Jeffery, *Nature*, 1947, **159**, 1620.
[16] Ferrari and Colla, *Atti Accad. Lincei*, 1930, **11**, 755; 1932, **14**, 435.

field case of cobalt(II) were not available in addition to the cobaltonitrites, but none of sufficiently substantiated constitution could be obtained. The value of θ for the two cobaltonitrites studied show a disagreement rather surprisingly large in view of the high degree of similarity that one expects between the environments of the cobalt atoms in the compounds. Once again, although the magnetic complexity is not sufficiently great to affect the conclusion that orbital contribution is negligible for the system, it is obvious that the ground state is not entirely simple. The assumption that the unpaired electron is accommodated in a pure d_{z^2} orbital must not be taken literally.

(d) *Quadricovalent spin-paired.* Apart from the phthalocyanine derivative, known from *X*-ray evidence to be square planar, in common with all the other phthalocyanines,[15] structural information is lacking for the compounds of the tetraco-ordinated spin-paired type; the assignment of a square stereochemistry is made principally on magnetic evidence. For the compound [Co(ethylenedi-iminebis-salicylaldehyde)][9], for which the values of θ of 60° and 0° (according as the form was " active " or " inactive " as an oxygen carrier) have been reported;[11] we find the value of 25°. The values of θ found for the other compounds of the square type were 10, 17, and, perhaps, 60°. The value of 60° is that assigned to the phthalocyanine derivative but the significance of the quantity in connection with this compound is a matter of conjecture, for the magnetic behaviour is quite anomalous. The variation of the susceptibility with temperature may be described by means of an expression of the form of a Curie–Weiss law in combination with a large term for the susceptibility independent of temperature, but probably not much physical significance can be attached to the individual terms of the expression; the moment at 80° K agrees with that calculated from the paramagnetic resonance *g* values taken at 14° K.[17] The remaining θ values again are of an order of magnitude which indicates some appreciable lack of magnetic simplicity in the ground state of the system but do not much affect the moment. The orbital contribution to the moment in these compounds is obviously not very dependent on temperature. The origin of the large orbital contribution in the square-planar type compounds is still not understood. The simple application of ligand-field theory discussed earlier does not satisfactorily account for moments of more than about 2·0 B.M. The theory neglects the possibility of the octahedral positions' being effectively filled, at least to some extent, by atoms other than ligands directly bonded to the metal atom in the solid state. This effect could drastically affect the assignment of levels given in Fig. 1, particularly in raising the energy of the d_{z^2} orbital in relation to the others. The effects produced by π bonding could also be of more importance in determining the distribution of the magnetic electrons than in the octahedral case. These considerations have recently been discussed in detail in reference to some phthalocyanines.[17]

The conclusion reached from the study of the available information on the temperature-dependence of the susceptibility of bivalent cobalt compounds is that the association of the presence of an orbital contribution to the moment with certain conditions of stereochemistry and bond type is confirmed. However, there does not seem to be the difference in the magnetic complexity of the ground states of the systems that do and do not give rise to this orbital contribution that the theory of the effect suggests.

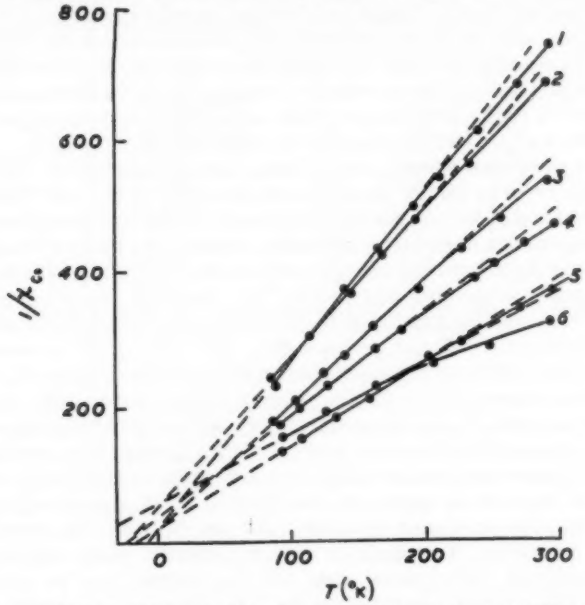
The small curvature in the susceptibility–temperature curves for the one unpaired-electron type compounds at higher temperatures is due to the presence of a small term independent of temperature, of the order of 60×10^{-6} i.g.s.u./mole, in the susceptibility. This effect will be discussed in detail in a later Part. It was not appreciable in the three unpaired electron case, as the Curie law susceptibilities then are so much larger.

Experimental

The temperature-dependence of the magnetic susceptibility was measured as described in Part I (preceding paper). The inverse of the corrected molar susceptibility is plotted against the temperature in Figs. 2 and 3. In Table 2 the corrections for diamagnetism, the moments

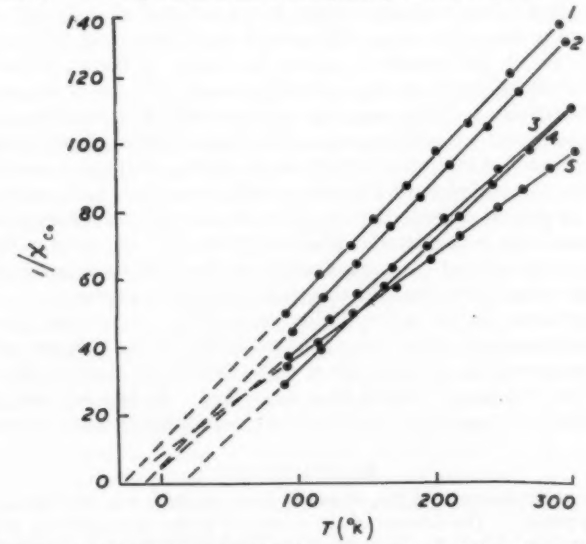
[17] Griffith, Gibson, Ingram, and Scholand, *Discuss. Faraday Soc.*, Dublin, September, 1958.

FIG. 2. *Inverse of corrected molar susceptibility* versus *temperature.*



1, $K_2PbCo(NO_2)_6$; 2, $K_2BaCo(NO_2)_6$; 3, $Co(o\text{-phenylenebisdimethylarsine})_3(ClO_4)_2$; 4, Co(ethylene-di-iminebis-salicylaldehyde); 5, Co(ethylthiopropanethiol); 6, Co(phthalocyanine).

FIG. 3. *Inverse of corrected molar susceptibility* versus *temperature.*



1, $Co(Ph{\cdot}NH_2)_2Cl_2$; 2, $HgCo(CNS)_4$; 3, $KCo(acetylacetone)_3$; 4, $Co(o\text{-phenanthroline})_3(ClO_4)_2$; 5, $(NH_4)_2Co(SO_4)_2,6H_2O$.

at the extremes of the temperature range, values of θ, and the accuracy of the measurement of the relative susceptibility at different temperatures are given. Corrections for the diamagnetic portions of the molecule were obtained either from Pascal's constants or by direct measurement of the diamagnetic portion of the molecule. No correction was included for the diamagnetism of the paired electrons of the filled shells of the cobalt atom itself. Values of θ were obtained by extrapolating the lower-temperature part of the inverse susceptibility–temperature curve to infinite susceptibility; the intercept on the temperature axis then gave the negative of θ.

"AnalaR" $(NH_4)_2Co(SO_4)_2.6H_2O$ was used. Specimens of $[Co(o\text{-phenanthroline})_3][ClO_4]_2$ and $[Co(o\text{-phenylenebisdimethylarsine})_3][ClO_4]_2$ were kindly supplied by Dr. C. Harris (University of New South Wales, Sydney). The specimens of [Co(phthalocyanine)][9], purified by repeated high-vacuum sublimation, and [Co(ethylthiopropanethiol)][9] were kindly supplied by Mr. P. Fielding and Dr. S. Livingstone respectively of that University. The specimen of $K[Co(acetylacetone)_3]$ was lent by Mr. A. Sargeson (University of Sydney). The cobaltonitrites were prepared as described in the literature,[18,19] with care during the preparation and subsequent handling to prevent oxidation. $[Co(Ph{\cdot}NH_2)_2Cl_2]$[9] and $HgCo(CNS)_4$ were prepared by mixing together the constituents in alcoholic and aqueous solutions respectively. [Co(ethylenediaminebis-salicylaldehyde)][9] was prepared by adding equimolar proportions of cobaltous chloride and the ligand in alcohol; the preparation, handling, and measurement of the susceptibility were conducted in an atmosphere of nitrogen to prevent oxidation of the sample.[20] These precautions were not necessary with the other compounds of the square type, which were chosen in order to avoid the effect.

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[18] Cuttica and Garobbi, *Gazzetta*, 1922, **52**, 270; Cuttica and Paoletti, *ibid.*, p. 279; Cuttica, *ibid.*, 1923, **53**, 185.
[19] Ray and Sahu, *J. Indian Chem. Soc.*, 1946, **23**, 161.
[20] Bailes, Calvin, and Wilmarth, *J. Amer. Chem. Soc.*, 1946, **68**, 2253

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62. *Steroids and Walden Inversion. Part XLI.* The Deamination of Some* A-*Nor-*, B-*Nor-, and* 17-*Amino-steroids.*

By C. W. SHOPPEE and J. C. P. SLY.

Amino-groups attached to flexible five-membered carbocyclic systems, *e.g.*, *cyclo*pentane, *cis*-perhydroindane, appear to possess mixed equatorial-axial character. Amino-groups attached to rigid five-membered carbocyclic systems, *e.g.*, *trans*-perhydroindane, or to such systems forming part of the nuclei of A-nor-5α-, A-nor-5β-, and 14α-steroids, at positions adjacent to a bridgehead, appear to possess either equatorial character disclosed by deamination with retention of configuration, or axial character disclosed by deamination with ready and exclusive elimination (Saytzew orientation); nor-steroids with amino-groups not adjacent to a bridgehead, like aliphatic amino-groups, undergo deamination with predominant inversion of configuration accompanied by some elimination.

PREVIOUS studies[1,2] of the stereochemical course of deamination of amino-steroids in aqueous acetic acid disclosed an unexpected divergence from the steric behaviour of amino-*cyclo*hexanes and aminodecalins. For all three groups of compounds the reaction is conformationally specific: equatorial amines undergo deamination with retention of

* Part XL, *J.*, 1958, 3048.

[1] Shoppee, Evans, and Summers, *J.*, 1957, 97.
[2] Shoppee, Cremlyn, Evans, and Summers, *J.*, 1957, 4364.

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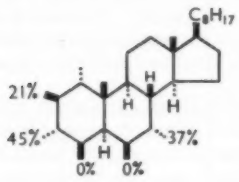
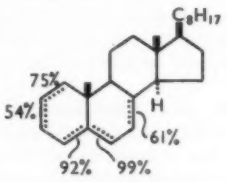
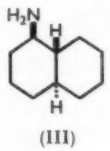
configuration but, whereas axial steroid amines display complete retention accompanied by elimination, axial amino*cyclo*hexanes and axial aminodecalins exhibit nearly complete inversion with concomitant elimination.[3,4]



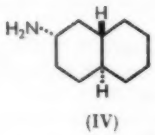
(I)



(II)

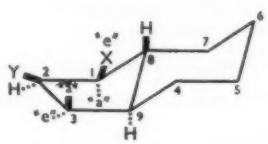


(III)

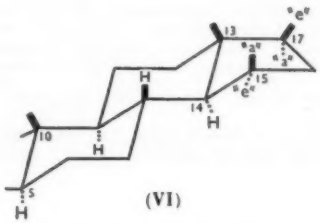


(IV)

Thus the axial 2β-, 3α-, 4β-, 6β-, and 7α-amino-5α-cholestanes * (I; substituent = NH_2) furnish with preservation of configuration the corresponding axial alcohols (I; substituent = OH) in the yields shown in (I), accompanied by the appropriate olefins, formed in accordance with the Saytzew orientation, in the yields indicated in (II).[1,2] By contrast, *cis*-1-amino-*trans*-decalin (III; NH_2, axial) and *trans*-2-amino-*trans*-decalin (IV; NH_2, axial) both yield 27% of the appropriate alcohol with the inverted configuration, and only 3% of that with the retained configuration, accompanied by 70% of olefins.[4]



(V) ‡§



(VI)

The principal mechanical difference between the polycyclic steroid nucleus (I) and the *bicyclo*[4 : 4 : 0]decane structures (III, IV) is the greater conformational stiffness of the former, not only in regard to bond-rotation, but also in respect of bond-angle deformation. *cyclo*Pentane is non-planar,[5] and therefore must possess some small degree of conformational flexibility; this is, however, so limited that *trans*-fusion to a single *cyclo*hexane ring ‡ (V), or to a multi*cyclo*hexane ring system (VI), produces an inflexible system. It was therefore of interest to prepare some A-nor-, B-nor-, and 17-amino-steroids and to examine the stereochemistry of their deamination.

Unlike the *trans*-perhydroindane system (V), the *cis*-perhydroindane system (VII, VIII) possesses flexibility which permits a 1-substituent (and in the case of an 8-methyl-*cis*-perhydroindane, a 3-substituent) to acquire either equatorial or axial character. Transformation occurs through systems in which the six-membered ring assumes the boat conformation: (i) a boat form with ends at $C_{(4)}$ and $C_{(7)}$ furnishing a structure with a plane of symmetry, or (ii) equivalent boat forms with ends at $C_{(5)}$ and $C_{(8)}$, or at $C_{(6)}$ and $C_{(9)}$.

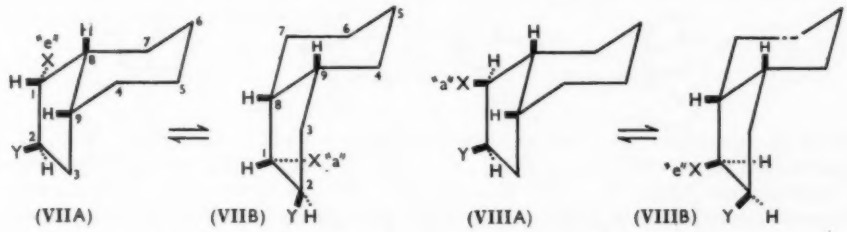
* Use of 5α- and 5β-cholestane in place of cholestane and coprostane, respectively, follows the I.U.P.A.C. 1957 Nomenclature Rules for Steroids (I.U.P.A.C. 1957 Rules for Organic Nomenclature, Butterworths, London, 1958) (cf. *J.*, 1958, 3458).

‡ This system is inflexible apart from transformation of the six-membered ring into boat conformations with ends (i) at $C_{(5)}$ and $C_{(8)}$, or (ii) at $C_{(6)}$ and $C_{(9)}$, neither of which affects the geometry at the bridgehead positions.

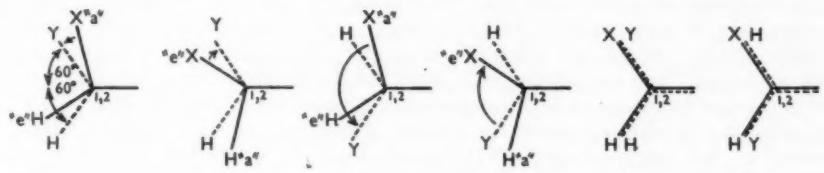
§ This structure represents one of a pair of stereoisomers.

[3] Mills, *J.*, 1953, 260; Bose, *Experientia*, 1953, **9**, 256.
[4] Dauben, Tweit, and Mannerskantz, *J. Amer. Chem. Soc.*, 1954, **76**, 4420.
[5] Kilpatrick, Pitzer, and Spitzer, *ibid.*, 1947, **69**, 2483.

The preferred conformation of *cyclo*pentane [6] possesses C_2 symmetry, and has $C_{(2)}$, $C_{(4)}$, and $C_{(5)}$ coplanar, with $C_{(1)}$ lying above that plane and $C_{(3)}$ lying an equal distance below that plane. This arrangement requires rotation of $C_{(1)}$ and $C_{(3)}$ in (V, VII, and



VIII) [and of $C_{(15)}$ and $C_{(17)}$ in (VI)] through equal and opposite angles, and permits staggering of bonds attached to the adjacent atoms $C_{(1)}$ and $C_{(2)}$ [and $C_{(3)}$](A, B, C, D), as compared with the eclipsed disposition of the bonds in a planar *cyclo*pentane system (E, F).



θ is the angle (=78°) between the two substituent bonds [$C_{(1)}$–X, $C_{(2)}$–Y] when projected on to a plane perpendicular to the $C_{(1)}$–$C_{(2)}$ bond-axis.

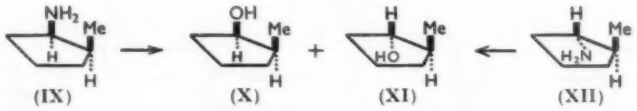
Substituents at $C_{(1)}$ [and, when appropriate, at $C_{(3)}$] in *trans*-perhydroindanes (V), *cis*-perhydroindanes (VII, VIII), and A-norsteroids should accordingly possess equatorial or axial character in the same way as 17-substituted steroids.[7]

Deamination in a simple *cyclo*pentane system can be exemplified by the work of Hückel and Kupka.[8] *cis*-1-Amino-2-methyl*cyclo*pentane (IX) yields 54% of the *cis*-alcohol (X), 23% of the *trans*-alcohol (XI), and 23% of olefins, whilst *trans*-1-amino-2-methyl*cyclo*pentane (XII) affords 32% of each of the epimeric alcohols (X, XI) and 35% of olefins. This reaction pattern recalls that of the epimeric amino*cyclo*hexanes and aminodecalins (see p. 345) and suggests the operation of conformational influences. It may be significant that, whereas in the *cis*-epimer (IX) steric compressions are equal in conformations (A) and (B) [X = NH_2, Y = Me], in the *trans*-epimer (XII) such compressions are less in conformation (C) [X = NH_2, " axial "] than in conformation (D) [X = NH_2, " equatorial "], leading to the development of more axial character in (XII) and resulting in less retention, more inversion, and more elimination.

The deamination of aminoperhydroindanes has been investigated by Hückel *et al.*[9] The symmetry of the *trans*-perhydroindane system (V) permits the existence of only a single racemic 2-substituted derivative. *trans*-Perhydroindan-2-one and its oxime by reduction, with sodium–ethanol or catalytically, give 2-hydroxy-*trans*-perhydroindane

[6] Le Fèvre and Le Fèvre, *J.*, 1956, 3549; Brutcher, Roberts, Barr, and Pearson, *J. Amer. Chem. Soc.*, 1956, **78**, 1507.
[7] Barton, *Experientia*, 1950, **6**, 316.
[8] Hückel and Kupka, *Chem. Ber.*, 1956, **89**, 1694.
[9] Hückel, Sachs, Yantschulewitsch, and Nerdel, *Annalen*, 1935, **518**, 155; Hückel, *ibid.*, 1937, **33**, 1.

(V; X = H, Y = OH) and 2-amino-*trans*-perhydroindane (V; X = H, Y = NH_2) respectively. Deamination of the latter gives the former together with a little unsaturated hydrocarbon,[9] so that here a mechanistically complete inversion would be observed as



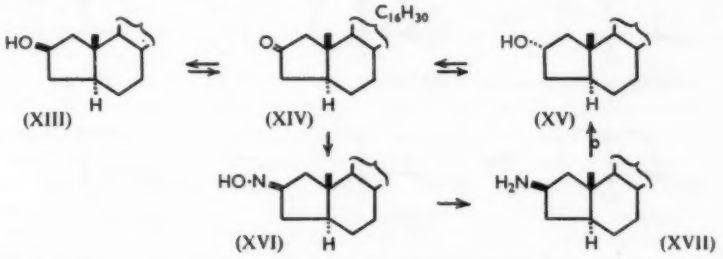
complete retention. *cis*-1-Amino-*cis*-perhydroindane (VII; X = NH_2, Y = H) by deamination gives ~52% of *cis*- (VII; X = OH, Y = H), ~13% of *trans*-1-hydroxy-*cis*-perhydroindane (VIII; X = OH, Y = H), and ~35% of olefins. The epimeric *trans*-1-amino-*cis*-perhydroindane (VIII; X = NH_2, Y = H) by deamination gives, however, only ~7% of the alcohol (VIII; X = OH, Y = H) with retained configuration, but yields ~63% of the alcohol (VII; X = OH, Y = H) with inverted configuration, and ~30% of olefins.[9] These results resemble those given by the 1-amino-2-methyl*cyclo*pentanes (IX, XII) and again suggest that conformational influences are operative. Conformational analysis shows that the number of molecules of *trans*-1-amino-*cis*-perhydroindane in conformation (VIIIA; NH_2, " axial ") as compared with conformation (VIIIB; NH_2, " equatorial ") depends only on the relative energy difference associated with an " axial " and an " equatorial " bond, but that stereoelectronic interactions compel the number of molecules of *cis*-1-amino-*cis*-perhydroindane in conformation (VIIA; NH_2, " equatorial ") greatly to exceed the number of molecules in conformation (VIIB; NH_2, " axial "). The amino-group in (VII) should therefore possess less axial character than that in (VIII), so that, by analogy with the reaction pattern characteristic of amino*cyclo*hexanes and aminodecalins, deamination of form (VII) should lead to more retention and less inversion (Found: ~52%, ~13%) than in the case of form (VIII) (Found: ~7%, ~63%). The epimeric 2-amino-*cis*-perhydroindanes should possess neither equatorial nor axial character and on deamination might be expected to exhibit the reaction pattern of aliphatic amines—predominant inversion with some elimination;[10] the single known 2-amino-*cis*-perhydroindane, which may be either *trans*- (VII ≡ VIII; X = H, Y = NH_2) or *cis*-2-amino-*cis*-perhydroindane (VII ≡ VIII; X = H, Y = NH_2 but with configuration at $C_{(2)}$ reversed), by deamination gives 80% of the alcohol with inverted configuration, 20% of the alcohol with retained configuration, and unsaturated hydrocarbon in undetermined amount.[9]

The present study involves the preparation of A-nor-5α-cholestan-1- and -2-one, and A-nor-5β-cholestan-1-, -2-, and -3-one, and, by way of their oximes, the five derived pairs of epimeric primary amines; we now report that part of this programme which has been realised.

A-Nor-5α-cholestan-2-one[11] (XIV) by reduction with sodium–ethanol or aluminium *iso*propoxide–propan-2-ol, or by hydrogenation in presence of platinum in acetic acid, gives a mixture of epimeric alcohols. One epimer,[12] m. p. 130°, $[\alpha]_D$ +38°, giving an insoluble digitonide and forming the major product of sodium–ethanol reduction, has been regarded as A-nor-5α-cholestan-2β-ol by analogy with 5α-cholestan-2β-ol,[13] and with the compound, m. p. 148°, $[\alpha]_D$ +2°, provisionally considered to be A-nor-5α-androstan-2β-ol,[14] which also afford insoluble digitonides. The other epimer, m. p. 155°, $[\alpha]_D$ + 28°, giving no insoluble digitonide and forming the major product of Meerwein–Ponndorf reduction,

[10] Brewster, Hiron, Hughes, Ingold, and Rao, *Nature*, 1950, **166**, 178.
[11] (*a*) Windaus and Dalmer, *Ber.*, 1919, **52**, 162, 170; Langer, *Z. physiol. Chem.*, 1933, **216**, 189; (*b*) Lettré, *ibid.*, 1933, **221**, 73.
[12] Kawasaki, *J. Pharm. Soc. Japan.*, 1936, **56**, 896; Marker, Kamm, Jones, and Mixon, *J. Amer. Chem. Soc.*, 1937, **59**, 1363.
[13] Ruzicka, Plattner, and Furrer, *Helv. Chim. Acta*, 1944, **27**, 727; Fürst and Plattner, *ibid.*, 1949, **32**, 275.
[14] Ruzicka, Prelog, and Meister, *ibid.*, 1945, **28**, 1651.

has been regarded as A-nor-5α-cholestan-2α-ol by analogy with 5α-cholestan-2α-ol,[13] and the substance, m. p. 121°, $[\alpha]_D$ +3°, provisionally considered to be A-nor-5α-androstan-2α-ol.[14] The ketoxime (XVI) by reduction with sodium and pentyl alcohol, or by hydrogenation (platinum–acetic acid), gave a single 2-amino-A-nor-5α-cholestane, characterised as the crystalline acetyl derivative.



Digitonide formation is a function of the crystal lattice, and an unreliable guide to molecular configuration;[15] it is, however, generally agreed that molecular rotatory power can give reliable indications of configuration.[16] Klyne's principle of enantiomeric types[16] cannot be used to indicate the configurations of the epimeric A-nor-5α-cholestan-2-ols because both ΔOH(16α) and ΔOH(16β) are negative and similar in magnitude (−33°, −20°), so that both ΔOH(2α : A-nor-5α) and ΔOH(2β : A-nor-5α) are expected to be positive and similar in size. The optical rotatory properties of the A-nor-5α-cholestane ($[M]_D$ +90°) and 5α-cholestane ($[M]_D$ +91°) systems are however closely similar, and the molecular rotations and molecular-rotation differences for (*a*) the epimeric A-nor-5α-cholestan-2-ols and 5α-cholestan-2-ols and their acetates,[13] and (*b*) the single 2-amino-A-nor-5α-cholestane, the epimeric 2-amino-5α-cholestanes,[2] and their acetyl derivatives [2] are given in the Table. The sign of the increments ΔM_D(OAc) appear especially significant. The ΔOAc values strongly suggest that the accepted configurations of the A-nor-5α-cholestan-2-ols should be reversed; the epimer, m. p. 130°, is A-nor-5α-cholestan-2α-ol (XV), whilst the epimer, m. p. 155°, is A-nor-5α-cholestan-2β-ol (XIII). These new assignments are consistent with the reduction of the ketone (XIV) by sodium–ethanol to afford 75% of the 2α- (XV) and 25% of the 2β-alcohol (XIII); provided that equilibration occurs, these figures give a measure of the relative thermodynamic stabilities of the epimers, which must reflect the 1 : 3-interactions [(XV; 2α-OH/5α-H), (XIII; 2β-OH/10β-Me)] since these constitute their sole conformational difference. It seems probable that the configurations provisionally assigned [14] to the epimeric 5α-androstan-2-ols may have likewise to be reversed.

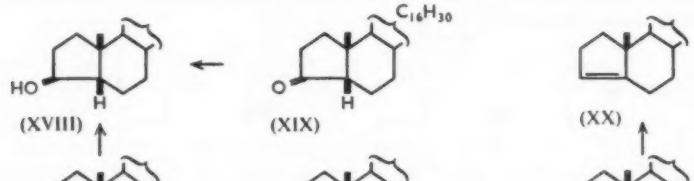
Compound	$[M]_D$ ROH	$[M]_D$ RH	ΔM_D OH	$[M]_D$ ROAc	$[M]_D$ RH	ΔM_D (OAc)
A-Nor-5α-cholestan-2α-ol, m. p. 130°	+142°	+90°	+52°	+4°	+90°	−86°
A-Nor-5α-cholestan-2β-ol, m. p. 155°	+105	+90	+15	+104	+90	+14
5α-Cholestan-2α-ol	+101	+91	+10	+61	+91	−30
5α-Cholestan-2β-ol	+132	+91	+41	+114	+91	+23
	R·NH_2	RH	NH_2	R·NHAc	RH	NHAc
2β-Amino-A-nor-5α-cholestane	+93	+90	+3	+162	+90	+72
2α-Amino-5α-cholestane	+77	+91	−14	−61	+91	+152
2β-Amino-5α-cholestane	+110	+91	+19	+118	+91	+27

The Δ values also suggest that the base obtained by reduction of the ketoxime (XVI) is 2β-amino-A-nor-5α-cholestane (XVII). This by deamination furnishes 93% of A-nor-5α-cholestan-2α-ol (XV) with 3% of unsaturated hydrocarbon (probably a mixture of

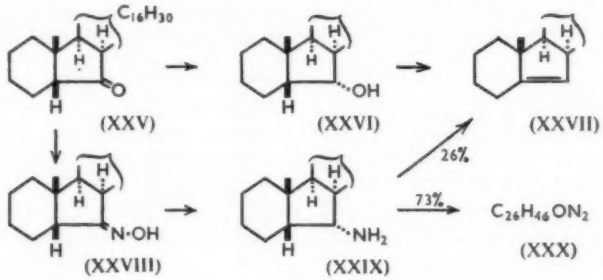
[15] Shoppee, in Robinson and Rodd's "Chemistry of Carbon Compounds," Elsevier Publ. Co., 1953, Vol. II*B*, p. 804.
[16] Klyne, *J.*, 1952, 2916.

A-nor-5α-cholest-1- and -2-ene); thus deamination here appears to proceed with substantially complete inversion of configuration.

A-Nor-5β-cholestan-3-one [11] (XIX) resisted hydrogenation in presence of platinum in



acetic acid–perchloric acid, but was reduced by sodium and pentyl alcohol or by lithium aluminium hydride in ether at 36° to 3β-hydroxy-A-nor-5β-cholestane (XVIII; OH, "equatorial"). The ketoxime (XXII) was reduced by sodium and pentyl alcohol to give 3β-amino-A-nor-5β-cholestane (XXI; NH_2, "equatorial"), and smoothly hydrogenated (platinum–acetic acid) to 3α-amino-A-nor-5β-cholestane (XXIII; NH_2, "axial"). Deamination of the 3β-amine gave, with retention of configuration, 40% of the 3β-alcohol (XVIII) accompanied by 59% of A-norcholest-3(5)-ene [11b] (XX); deamination of the 3α-amine (XXIII) furnished ~100% of the hydrocarbon (XX), unaccompanied by alcohol.

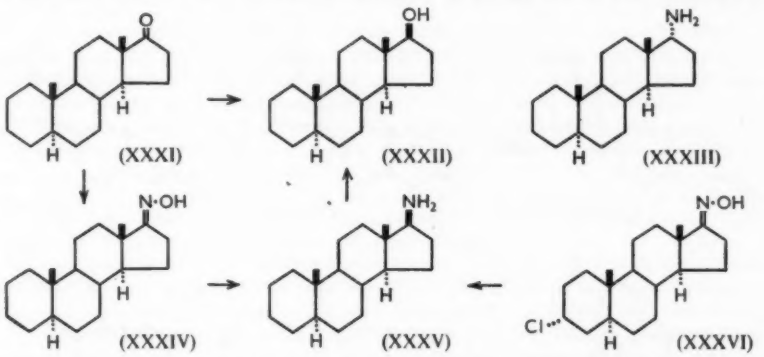


Barium 6 : 7-*seco*-5α-cholestane-6 : 7-dioate on pyrolysis at 400°/1 mm. yields a ketone,[17] which we formulate as B-nor-5β : 8α-cholestan-6-one (XXV) on the grounds that *cis*-perhydroindan-1-one [9] and *cis*-perhydroindan-4-one [18] are more stable than their *trans*-isomerides. Ring B then conforms to the Le Fèvre model for *cyclo*pentanone [6] with $C_{(6)}$, $C_{(9)}$, and $C_{(10)}$ coplanar, and $C_{(5)}$ below and $C_{(8)}$ above that plane; the 6β-position is greatly hindered by the 10β-methyl group, the 11β-hydrogen atom, and the 13β-methyl group, whilst the 6α-position is relatively unhindered. The ketone (XXV) by reduction with sodium and pentyl alcohol or with lithium aluminium hydride gives a single alcohol, which we accordingly regard as B-nor-5β : 8α-cholestan-6α-ol (XXVI), readily dehydrated by thionyl chloride–pyridine at 20° to B-nor-8α-cholest-5-ene (XXVII). The ketoxime [17] (XXVIII) resisted catalytic hydrogenation, but was reduced by sodium and pentyl alcohol or by lithium aluminium hydride to a single amine, which we formulate by analogy with the alcohol (XXVI) as 6α-amino-B-nor-5β : 8α-cholestane (XXIX). Deamination of this base gave 26% of B-nor-8α-cholest-5-ene (XXVII) accompanied by 73% of a colourless compound, $C_{26}H_{46}ON_2$, double m. p. 121°/136° (XXX), whose infrared absorption spectrum

[17] Stange, *Z. physiol. Chem.*, 1933, **218**, 74.
[18] Dimroth and Jonsson, *Ber.*, 1941, **74**, 520.

showed no characteristic absorption bands [the nitroso-group furnishes intense bands: C–N:O, 1310—1420 or 1350—1400; N–N:O, 1400 and 1653; O–N:O, 1613—1625 and 1653—1681 cm.$^{-1}$]. One of the two nitrogen atoms of compound (XXX) appears to be the original amino-nitrogen atom, whilst the other must be derived from the nitrosonium ion NO^+; the only primary nitrosamines, Ar·NH·NO, are yellow unstable substances.[19] An addition compound of dinitrogen trioxide and the hydrocarbon (XXVII), or an isomeride arising by rearrangement, is excluded by the presence of only one oxygen atom in (XXX).

5α-Androstan-17-one [20] (XXXI) by reduction with sodium and pentyl alcohol [21] or with lithium aluminium hydride [22] affords almost exclusively 5α-androstan-17β-ol [20,23] (XXXII); similarly, the ketoxime (XXXIV) by reduction with sodium and ethanol, lithium aluminium hydride, or hydrogen–platinum–acetic acid gives exclusively the crystalline 17β-amino-5α-androstane (XXXV; NH_2, "equatorial"); this is probably identical with the base, b. p. 110°/0·01 mm., obtained from 3α-chloro-5α-androstan-17-one oxime (XXXVI) by reduction with sodium and pentyl alcohol.[21] Deamination of 17β-amino-5α-androstane (XXXV) gives with complete retention and in almost



quantitative yield 5α-androstan-17β-ol (XXXII) (cf. ref. 21). Attempts to prepare 17α-amino-5α-androstane (XXXIII) by treatment of 5α-androstan-17β-yl toluene-*p*-sulphonate at 100° with ammonia, alone or in the presence of sodamide, failed; Elkes and Shoppee [22] found similarly that acetolysis gave only about 5% of 17α-acetoxy-5α-androstane.

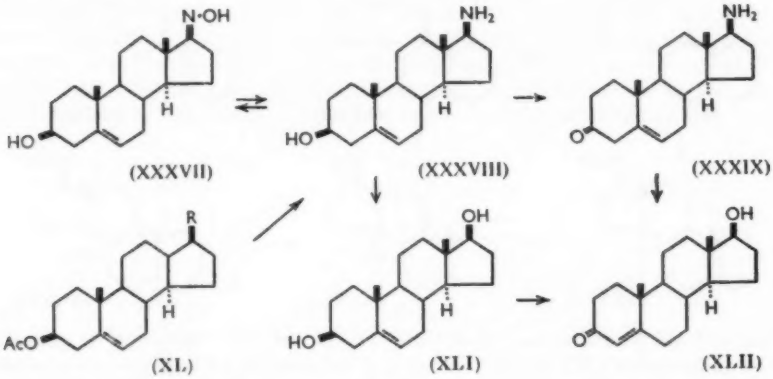
Androsterone oxime by reduction with sodium and ethanol [21,24] or catalytically [24] gives 17β-amino-5α-androstan-3α-ol, also obtained from 3α-acetoxy*allo*etianic acid as the azide by the Curtius rearrangement, in which the configuration of the migrating group is known to be preserved,[25] and hydrolysis of the resulting 17β-*iso*cyanate. Deamination of 17β-amino-5α-androstan-3α-ol proceeds with retention of configuration to yield 5α-androstane-3α : 17β-diol.[21,26] Dehydro*epi*androsterone oxime (XXXVII) by reduction with sodium and ethanol gives 17β-aminoandrost-5-en-3β-ol [27] (XXXVIII), which we have also obtained by use of lithium aluminium hydride in ether at 36°. The base (XXXVIII) can be prepared [28,29] (*a*) from 3β-acetoxyeti-5-enic acid (XL; R = CO_2H) as the azide (XL;

[18] Hantzsch, *Ber.*, 1912, **45**, 3036; 1930, **63**, 1280.
[20] Rosenkranz, Kaufmann, and Romo, *J. Amer. Chem. Soc.*, 1949, **71**, 3689.
[21] Marker, *ibid.*, 1936, **58**, 480.
[22] Elks and Shoppee, *J.*, 1953, 241.
[23] Shoppee, *Chem. and Ind.*, 1950, 454.
[24] CIBA, B.P. 451,352/1936.
[25] (*a*) Jones and Wallis, *J. Amer. Chem. Soc.*, 1926, **48**, 169; (*b*) Kenyon and Campbell, *J.*, 1946, 25.
[26] CIBA, Swiss P. 191,339/1936; I.G. Farbenind., B.P. 478,583/1936.
[27] Ruzicka and Goldberg, *Helv. Chim. Acta*, 1936, **19**, 107.
[28] Schmidt-Thomé, *Chem. Ber.*, 1955, **88**, 895.
[29] CIBA, Swiss P. 193,468/1936; I.G. Farbenind., French P. 819,975/1937; 819,975/1939; B.P. 501,421/1937; Erhardt, Rushig, and Aumuller, *Angew. Chem.*, 1939, **52**, 363.

R = CON_3) by the Curtius rearrangement, to yield the 17β-*iso*cyanate (XL; R = NCO) and acid hydrolysis thereof, and (*b*) from pregnenolone acetate oxime (XL; R = CMe:N·OH) by the Beckmann rearrangement (in which the configuration of the migrating group is also known to be retained [25b, 30]) and subsequent hydrolysis; we have repeated these preparations and characterised the base (XXXVIII) by preparation of the 3β : 17β-diacetyl derivative.

Deamination of the 17β-amine (XXXVIII; NH_2, " equatorial ") occurs with complete retention of configuration, to yield androst-5-ene-3β : 17β-diol (XLI) (cf. patents in ref. 29). Similarly, 17β-aminoandrost-5-en-3-one (XXXIX; NH_2, " equatorial ") by deamination is reported [29] to give testosterone (XLII), with retention of configuration, whilst (+)-œstrone-b oxime by reduction with sodium and ethanol gives 17β-aminoœstra-1 : 3 : 5(10)-triene, deaminated with retention of configuration to œstradiol-17β.[31]

The foregoing evidence suggests that amino-groups attached to flexible five-membered carbocyclic systems, *e.g.*, *cyclo*pentane, *cis*-perhydroindane, possess mixed equatorial-axial character according to the conformational exigencies of the situation. Amino-groups attached to rigid five-membered carbocyclic systems, *e.g.*, *trans*-perhydroindane, or to such systems forming part of the nuclei of A-nor-5α- A-nor-5β-, and normal 14α-steroids, and



placed adjacent to a bridgehead appear to possess either equatorial character characterised by deamination with retention of configuration accompanied by some elimination (Saytzew orientation), or axial character characterised by deamination with ready and exclusive elimination (Saytzew orientation) [cf. 4β- and 6β-amino-5α-cholestane (NH_2, " axial ") which by deamination give 100% of cholest-4-ene and cholest-5-ene respectively [2]]; amino-groups not adjacent to a bridgehead appear to resemble aliphatic amino-groups and to undergo deamination with predominant inversion of configuration, accompanied by some elimination.

The complete absence of elimination products (derivatives of 5α-androst-16-ene or of ψ-androstene) in the deamination of 17β-amino-steroids (NH_2, " equatorial ") may reflect the presence of the angular 18-methyl group on the adjacent bridgehead carbon atom and suggests that the diazonium ion, rather than a carbonium ion, is the important intermediate.

Experimental

M. p.s were determined on a Kofler block and are therefore corrected (error ±2°). Solvents for chromatography were rigorously purified and dried, and, unless stated otherwise, aluminium

[30] Kenyon and Young, *J.*, 1941, 263.
[31] Schering A.G., G.P. 711,378/1932; B.P. 428,133/1933.

oxide (Spence type H, activity ~II) was used. The phrase " usual isolation " implies extraction with ether, washing with 2N-hydrochloric acid and/or 2N-sodium carbonate, and with water, and brief drying (Na_2SO_4). Ultraviolet absorption spectra were determined for ethanol solutions in a Hilger Uvispek spectrophotometer, and infrared absorption spectra were measured for carbon tetrachloride solutions in a Perkin-Elmer Model 21 double-beam instrument. $[\alpha]_D$ refer to chloroform solutions.

A-*Nor*-5α-*cholestan*-2-*one* (XIV).—Cholestanol (11 g.) was oxidised [32] with chromium trioxide (11·5 g.) in 90% acetic acid at 70—75° for 2·5 hr. to 2 : 3-*seco*-5α-cholestane-2 : 3-dioic acid (8·5 g.), m. p. 196—197° (from ether–pentane), which when refluxed with acetic anhydride and then distilled at 300°/1·5 mm. gave, after the usual work up, A-nor-5α-cholestan-2-one [11] (4·6 g.), m. p. 100—101° (from methanol) [oxime, m. p. 201—203° (from ethyl acetate)].

A-*Nor*-5α-*cholestan*-2α- *and* -2β-*ol* (XV, XIII).—A-Nor-5α-cholestan-2-one by reduction with excess of sodium in refluxing ethanol, or with aluminium *iso*propoxide in slowly distilling (7 hr.) propan-2-ol, gave a mixture of the epimeric alcohols, which were separated by treatment overnight with a 4% ethanolic solution of digitonin. The insoluble digitonide, on decomposition with pyridine, gave A-nor-5α-cholestan-2α-ol,[12] m. p. 128°, $[\alpha]_D$ +38° (*c* 1·2) {acetate, m. p. 80°, $[\alpha]_D$ +1° (*c* 0·8)}; the material not precipitated by digitonin gave, on recrystallisation from methanol, A-nor-5α-cholestan-2β-ol [12] as a solvate, m. p. 120° with transition to needles, m. p. >135°, which after sublimation at 160°/0·5 mm. had m. p. 153°, $[\alpha]_D$ +28° (*c* 1·0) {acetate, m. p. 93°, $[\alpha]_D$ +25° (*c* 0·4)}.

2β-*Amino*-A-*nor*-5α-*cholestane* (XVII).—(*a*) A-Norcholestan-2-one oxime (600 mg.) in refluxing pentyl alcohol (200 c.c.) was saturated with sodium during 2 hr.; after a further 1·5 hr., excess of sodium was destroyed with ethanol, and the basic product isolated in the usual way. The resultant oil (580 mg.) was chromatographed on a column of aluminium oxide (18 g.) prepared in benzene. Elution with benzene (7 × 60 c.c.) gave unchanged oxime (109 mg.); elution with ether, chloroform, and finally methanol yielded 2β-*amino*-A-*nor*-5α-*cholestane* (430 mg.), b. p. 150°/0·01 mm., $[\alpha]_D$ +25·5° (*c* 0·9) (Found: C, 83·3; H, 12·4. $C_{26}H_{47}N$ requires C, 83·55; H, 12·7%), converted by acetic anhydride into the *acetyl derivative*, m. p. 190—191° (from acetone), $[\alpha]_D$ +39° (*c* 1·0) [Found (after drying at 25°/0·03 mm. for 4 hr.): C, 80·5; H, 11·7; N, 3·1. $C_{28}H_{49}ON$ requires C, 80·9; H, 11·9; N, 3·4%].

(*b*) The ketoxime (500 mg.) was hydrogenated with platinum oxide (200 mg.) in acetic acid (50 c.c.); reaction was complete in 6 hr. After removal of acetic acid in a vacuum the base was isolated in the usual way and acetylated with acetic anhydride, and the solid product purified by chromatography on a column of aluminium oxide (15 g.) prepared in pentane. Elution with benzene–pentane (1 : 1; 6 × 50 c.c.) gave 2β-acetamido-A-nor-5α-cholestane (410 mg.), m. p. 189—191° (from acetone), identical with the specimen prepared as under (*a*) above.

A-*Nor*-5β-*cholestan*-3-*one* (XIX).—3 : 4-*seco*Cholest-5-ene-3 : 4-dioic acid [Diels's acid], m. p. 296°, was prepared by Diels and Abderhalden's method [33] as modified by Shoppee and Summers,[34] and converted by refluxing it with acetic anhydride and pyrolysing the product at 300—320°/1·5 mm. into A-norcholest-5-en-3-one, m. p. 95°, hydrogenated with palladium oxide in ether–acetic acid to A-nor-5β-cholestan-3-one, m. p. 74°. The *oxime* of the latter had m. p. 129—130°, $[\alpha]_D$ +74° (*c* 0·9), after crystallisation from methanol [Found (after drying at 20°/0·03 mm. for 8 hr.): C, 80·55; H, 11·4. $C_{26}H_{45}ON$ requires C, 80·55; H, 11·7%].

A-*Nor*-5β-*cholestan*-3β-*ol* (XVIII).—(*a*) A-Nor-5β-cholestan-3-one (250 mg.) in refluxing ethanol was treated with an excess of sodium during 2 hr.; the usual isolation gave an oil (240 mg.), which was chromatographed on a column of aluminium oxide prepared in benzene. Elution with ether–benzene (1 : 9, 3 × 20 c.c.; 1 : 4, 3 × 20 c.c.) gave A-*nor*-5β-*cholestan*-3β-*ol* (200 mg.), double m. p. 89°/107° (from methanol), $[\alpha]_D$ +51° (*c* 0·9) [Found (after drying at 25°/0·5 mm. for 12 hr.): C, 83·0; H, 12·0. $C_{26}H_{46}O$ requires C, 83·35; H, 12·35%].

(*b*) The ketone (85 mg.) was refluxed with lithium aluminium hydride (50 mg.) in ether for 1 hr. to yield, after the usual isolation procedure, an oil (85 mg.), which by chromatography as under (*a*) furnished A-nor-5β-cholestan-3β-ol (69 mg.), m. p. and mixed double m. p. 89°/106°.

The ketone (100 mg.) resisted hydrogenation in presence of platinum oxide (44 mg.) in ether–acetic acid (1 : 4; 20 c.c.) containing 2 drops of 60% perchloric acid, and was recovered unchanged (97 mg.; m. p. and mixed m. p. 74°).

[32] Cf. Windaus and Uibrig, *Ber.*, 1914, **47**, 2384.
[33] Diels and Abderhalden, *Ber.*, 1903, **36**, 3177.
[34] Shoppee and Summers, *J.*, 1952, 2528.

3α-*Amino-* *and* 3β-*Amino*-A-*nor*-5β-*cholestane* (XXIII, XXI).—(*a*) The ketoxime (XXII) (600 mg.) in refluxing pentyl alcohol (120 c.c.) was saturated with sodium during 3 hr. After another hour, excess of sodium was destroyed with ethanol, and the solution poured into water, and extracted with ether; working up through the ether-insoluble hydrochloride gave 3β-amino-A-nor-5β-cholestane (400 mg.), b. p. 181—185°/0·5 mm., $[\alpha]_D$ +46° (*c* 0·8) (Found: C, 83·4; H, 12·8; N, 3·62. $C_{26}H_{47}N$ requires C, 83·55; H, 12·7; N, 3·75%). Acetic anhydride afforded the *acetyl derivative*, m. p. 246—247°, $[\alpha]_D$ +48° (*c* 0·9), after recrystallisation from acetone [Found (after drying at 20°/0·03 mm. for 20 hr.): C, 80·6; H, 11·75. $C_{28}H_{49}ON$ requires C, 80·9; H, 11·9%].

(*b*) The ketoxime (250 mg.) was hydrogenated in presence of platinum oxide (100 mg.) in acetic acid (35 c.c.) in 0·75 hr. The base was isolated in the usual way as an oil (220 mg.) and chromatographed on a column of aluminium oxide (7 g.) prepared in benzene. Elution with ether–benzene, ether, chloroform, and finally methanol gave 3α-*amino*-A-*nor*-5β-*cholestane*, m. p. 66—68° (from methanol), $[\alpha]_D$ +9° (*c* 1·1) [Found (after distillation at 150°/0·02 mm.): C, 83·2; H, 12·5. $C_{26}H_{47}N$ requires C, 83·55; H, 12·7%]. Acetic anhydride furnished the *acetyl derivative*, m. p. 166—168°, $[\alpha]_D$ +67° (*c* 0·9), after recrystallisation from acetone [Found (after drying at 20°/0·03 mm. for 20 hr.): C, 80·6; H, 11·6. $C_{28}H_{49}ON$ requires C, 80·9; H, 11·9%].

B-*Nor*-5β- : 8α-*cholestan*-6-*one* (XXV).—3β-Hydroxy-6 : 7-*seco*-5α-cholestane-6 : 7-dioic acid,[35,36] m. p. 239°, was oxidised with chromium trioxide in acetic acid to the 3-oxo-acid,[35,37] m. p. 254—255°, which by Clemmensen reduction gave only 27% of 6 : 7-*seco*-5α-cholestane-6 : 7-dioic acid.[37] The 3-oxo-acid (8·3 g.) was therefore refluxed in ethylene glycol (215 c.c.) containing hydrazine hydrate (7 c.c.) with sodium (8·3 g.) for 1 hr.; the temperature was allowed to rise to 185°, and refluxing continued for 6 hr.; working up gave 6 : 7-*seco*-5α-cholestane-6 : 7-dioic acid (7·3 g.), m. p. 272—273° (from acetic acid). The dry barium salt by pyrolysis at 400—420°/1·5 mm. for 3 hr. gave an oily distillate, which by the usual isolation procedure gave B-nor-5β : 8α-cholestan-6-one,[17] m. p. 92—93° (from aqueous acetone at 0°). The oxime[17] had m. p. 185—187° (from methanol).

B-*Nor*-5β : 8α-*cholestan*-6α-*ol* (XXVI).—(*a*) B-Nor-5β : 8α-cholestan-6-one (200 mg.) in refluxing pentyl alcohol (80 c.c.) was saturated with sodium during 1·5 hr.; after 2 hr., excess of sodium was destroyed with ethanol, and the mixture worked up in the usual way, giving an oil (170 mg.), which was chromatographed on a column of aluminium oxide (6 g.) prepared in pentane. Elution with benzene–pentane (1 : 1; 8 × 20 c.c.) afforded B-*nor*-5β : 8α-*cholestan*-6α-*ol* (144 mg.), m. p. 85—87°, $[\alpha]_D$ +42° (*c* 1·0) (from aqueous acetone) [Found (after drying at 25°/0·04 mm. for 20 hr.): C, 83·0; H, 12·0. $C_{26}H_{46}O$ requires C, 83·35; H, 12·35%].

(*b*) The ketone (300 mg.) in ether was refluxed with excess of lithium aluminium hydride for 14 hr. Excess of the reagent was destroyed with ice-water, and the ethereal solution worked up to give an oil (290 mg.); chromatography as under (*a*) gave by elution with pentane (6 × 30 c.c.) unchanged ketone (145 mg.), m. p. 92°, and by elution with benzene–pentane (1 : 1; 7 × 25 c.c.) B-nor-5β : 8α-cholestan-6α-ol (120 mg.), m. p. and mixed m. p. 85—87° (from aqueous acetone). The alcohol, on treatment with thionyl chloride–pyridine at 20° overnight, gave B-nor-8α-cholest-5-ene (XXVII), as an oil giving a yellow colour with tetranitromethane in chloroform, but the quantity was insufficient for purification.

6α-*Amino*-B-*nor*-5β : 8α-*cholestane* (XXIX).—(*a*) The ketoxime (XXVIII) (215 mg.) in refluxing pentyl alcohol was saturated with sodium during 2·5 hr.; refluxing was continued for 4 hr., excess of sodium destroyed with ethanol, the mixture poured into water, and the product isolated with ether. The resultant oil (200 mg.) was chromatographed on a column of aluminium oxide (6 g.) prepared in pentane. Elution with benzene–pentane (1 : 1), and benzene gave unidentified oils, but elution with benzene–ether (1 : 1), ether, and finally chloroform gave 6α-*amino*-B-*nor*-5β : 8α-*cholestane*, b. p. 220—230°/1 mm., $[\alpha]_D$ +33° (*c* 1·1) (Found: C, 83·1; H, 12·2. $C_{26}H_{47}N$ requires C, 83·55; H, 12·7%), converted by acetic anhydride into the *acetyl derivative*, which after distillation at 180—190°/0·4 mm. crystallised from acetone, then having m. p. 178—180°, $[\alpha]_D$ +14° (*c* 1·1) [Found (after drying at 25°/0·05 mm. for 12 hr.): C, 80·65; H, 11·8; N, 3·7. $C_{28}H_{49}ON$ requires C, 80·9; H, 11·9; N, 3·4%].

(*b*) The ketoxime (XXVIII) (110 mg.) in dioxan (30 c.c.) was refluxed with excess of lithium

[35] Windaus and Stein, *Ber.*, 1904, **37**, 3699.
[36] Shoppee, *J.*, 1948, 1032.
[37] Windaus and von Staden, *Ber.*, 1921, **54**, 1059.

aluminium hydride for 16 hr. After addition of ice-water and filtration of the precipitate of aluminium hydroxide, the filtrate was diluted with water and extracted with ether, to give by the usual isolation procedure an oil (110 mg.). This was acetylated with acetic anhydride and the product chromatographed on a column of aluminium oxide (4 g.) prepared in pentane. Elution with benzene and ether–benzene (1 : 4) and recrystallisation from acetone gave 6-acetamido-B-nor-5β : 8α-cholestane, m. p. and mixed m. p. 178—180°, with the specimen prepared as under (*a*) above.

The ketoxime (XXVIII) (120 mg.) resisted hydrogenation in presence of platinum oxide (50 mg.) in acetic acid (30 c.c.) containing 4 drops of 60% perchloric acid at 20° and at 55—60°, and was recovered unchanged (115 mg.; m. p. and mixed m. p. 186—188°).

17β-*Amino-5α-androstane* (XXXIV).—(*a*) *5α-Androstan-17-one oxime* (XXXIV) [m. p. 173—176° (from ether–methanol) (Found: N, 4·9. $C_{19}H_{31}ON$ requires N, 4·8%); 1 g.] in refluxing ethanol was saturated during 1 hr. with sodium excess of which was destroyed by adding ethanol. The cooled mixture was poured into saturated sodium chloride solution, and the base isolated, through the ether-insoluble hydrochloride, as an oil which on crystallisation from acetone gave 17β-amino-5α-androstane, m. p. 138—141° [Found (after sublimation at 130°/0·02 mm.): C, 82·65; H, 12·0. $C_{19}H_{33}N$ requires C, 82·85; H, 12·1%]. Treatment with acetic anhydride at 100° for 15 min. gave the *acetyl derivative*, m. p. 208—209° (from ethyl acetate) [Found (after sublimation at 180°/0·02 mm.): C, 79·25; H, 11·1. $C_{21}H_{35}ON$ requires C, 79·45; H, 11·1%].

(*b*) The ketoxime (XXXIV) (500 mg.) in ether (100 c.c.) was refluxed with lithium aluminium hydride (1 g.) for 3 hr. The usual working up gave 17β-amino-5α-androstane (480 mg.), m. p. and mixed m. p. 138—140° (from acetone).

(*c*) The ketoxime (XXXIV) (400 mg.) was hydrogenated in presence of platinum oxide (100 mg.) in acetic acid (50 c.c.) containing 2 drops of 60% perchloric acid. The reaction was complete in 1 hr., and after removal of acetic acid in a vacuum the base was isolated in the usual way, furnishing 17β-amino-5α-androstane (380 mg.), m. p. and mixed m. p. 138—141°.

17β-*Aminoandrost-5-en-3β-ol* (XXXVIII).—(*a*) 3β-Acetoxyandrost-5-en-17-one oxime (1·5 g.) in refluxing ethanol (100 c.c.) was treated with excess of sodium. The usual isolation gave 17β-aminoandrost-5-en-3β-ol (1·3 g.), m. p. 160° (from ethyl acetate), $[\alpha]_D$ −80° (*c* 1·0). Acetic anhydride at 140° afforded 17β-*acetamidoandrost-5-en-3β-yl acetate*, m. p. 196°, $[\alpha]_D$ −88° (*c* 0·5), after recrystallisation from ether–methanol [Found (after drying at 70°/0·02 mm. for 6 hr.): C, 70·8; H, 9·3; N, 3·4. $C_{23}H_{35}O_3N$ requires C, 70·9; H, 9·5; N, 3·6%].

(*b*) 3β-Acetoxyandrost-5-en-17-one oxime (500 mg.) in ether (50 c.c.) was refluxed with excess of lithium aluminium hydride for 3 hr. The usual isolation gave 17β-aminoandrost-5-en-3β-ol (450 mg.), m. p. 159—160° (from ethyl acetate) [Found (after drying at 70°/0·02 mm. for 6 hr.): C, 78·6; H, 11·5. Calc. for $C_{19}H_{33}ON$: C, 78·3; H, 11·4%].

(*c*) 3β-Acetoxyeti-5-enic acid (500 mg.) in benzene (20 c.c.) was refluxed with purified thionyl chloride (1 c.c.) for 2 hr. The chloride, obtained by complete evaporation in a vacuum, was dissolved in acetone–dioxan (2 : 1, 60 c.c.), and treated dropwise with a solution of sodium azide (300 mg.) in water (1·2 c.c.) with stirring. After 0·5 hr., water was added, and the precipitate filtered off, washed with water, and dried in a vacuum-desiccator overnight; this material was heated in benzene for 1·5 hr. to ensure conversion into the 17β-*iso*cyanate, which was hydrolysed by addition of acetic acid (20 c.c.) and concentrated hydrochloric acid (7 c.c.) and refluxing for 2 hr. After evaporation in a vacuum, the product was refluxed with 15% methanolic sodium hydroxide for 1 hr., and the base isolated through the ether-insoluble hydrochloride as an oil (245 mg.), which was chromatographed on a column of aluminium oxide (7 g.) prepared in pentane. Elution with benzene (4 × 25 c.c.) gave 17β-aminoandrost-5-en-3β-ol (175 mg.), m. p. and mixed m. p. 158—160°, identical with the specimens prepared as under (*a*) and (*b*) above, and characterised as the 3β : 17β-diacetyl derivative, m. p. 196°.

Deaminations.—In the following six experiments the steroid amine was dissolved in 50% acetic acid and where necessary dioxan was added to give complete dissolution. Sodium nitrite (approximately 2—3 times the weight of the amine) in 50% acetic acid was added dropwise with stirring at 20°, and the mixture left overnight. After basification with 4N-sodium hydroxide the product was isolated by extraction with ether, and then hydrolysed for 0·5 hr. with 5% methanolic potassium hydroxide, or acetylated with acetic anhydride at 100°.

(1) 2β-Amino-A-nor-5α-cholestane (XVII) (205 mg.) gave a product which, by chromatography on aluminium oxide (6 g.) prepared in pentane, yielded: (*a*) an oil (5 mg.; eluted with pentane), which did not crystallise satisfactorily, but gave a positive test for unsaturation

XUM

with tetranitromethane in chloroform, and is probably A-nor-5α-cholest-1- and/or -2-ene; (*b*) A-nor-5α-cholestan-2α-ol (XV) (125 mg.; eluted with ether–benzene (1 : 4, 1 : 1)], m. p. and mixed m. p. 128° after crystallisation from methanol; and (*c*) an oil (60 mg.; eluted with chloroform and methanol) which by acetylation gave 2β-acetamido-A-nor-5α-cholestane, m. p. and mixed m. p. 189° (from acetone).

(2) 3β-Amino-A-nor-5β-cholestane (XXI) (600 mg.) gave a product from which most of the basic material was separated by treatment with dry hydrogen chloride in ether. The ether-insoluble hydrochloride (290 mg.) yielded (on acetylation) 3β-acetamido-A-nor-5β-cholestane, m. p. and mixed m. p. 244—246° (from acetone). The residual material (315 mg.) by chromatography on aluminium oxide (10 g.) in pentane furnished: (*a*) A-norcholest-3(5)-ene [11b] (XX) (177 mg.; eluted with pentane), m. p. 80°, $[\alpha]_D$ +53° (*c* 1·1) {lit., m. p. 80°; $[\alpha]_D$ +55°} (after crystallisation from methanol); (*b*) A-nor-5β-cholestan-3β-ol (XXVIII) [119 mg.; eluted with benzene and ether–benzene (1 : 4)], double m. p. 88°/107° (from methanol) undepressed on admixture with an authentic specimen; and (*c*) oil (14 mg.; eluted with ether), which on acetylation gave 3β-acetamido-A-nor-5β-cholestane, m. p. and mixed m. p. 244—246° (from acetone).

(3) 3α-Amino-A-nor-5β-cholestane (XXIII) (210 mg.) gave a product (195 mg.) which, by chromatography on aluminium oxide in pentane, yield (*a*) A-norcholest-3(5)-ene (XX) (82 mg.; eluted with pentane), m. p. 79—80° (from methanol), and (*b*) oils (105 mg.; eluted with benzene, ether, and finally methanol), which on acetylation gave 3α-acetamido-A-nor-5β-cholestane, m. p. and mixed m. p. 165° (from acetone).

(4) 6α-Amino-B-nor-5β : 8α-cholestane (XXIX) (300 mg.) gave a product (280 mg.) which on chromatography on aluminium oxide (9 g.) furnished: (*a*) B-nor-8α-cholest-5-ene (XXVII) (50 mg.; eluted with pentane), which did not crystallise but gave a yellow colour with tetranitromethane in chloroform; (*b*) a *substance*, $C_{26}H_{46}ON_2$ [146 mg.; eluted with benzene–pentane (1 : 1) and benzene], which was crystallised with difficulty from aqueous acetone, then having double m. p. 121°/136—138° [Found (after drying at 20°/0·02 mm. for 12 hr.): C, 77·7; H, 11·7; O, 4·4; N, 6·7%; *M* (Rast), 390. $C_{26}H_{46}ON_2$ requires C, 77·55; H, 11·5; O, 4·0; N, 6·9%; *M*, 402]; and (*c*) an oil (75 mg.; eluted with ether and methanol), which on acetylation afforded 6α-acetamido-B-nor-5β : 8α-cholestane, m. p. and mixed m. p. 178° (from acetone). A second experiment gave a similar result.

(5) 17β-Amino-5α-androstane (XXXV) (130 mg.) yielded 5α-androstan-17β-ol (XXXII) (125 mg.), m. p. and mixed m. p. 168—170° (from hexane).

(6) 17β-Aminoandrost-5-en-3β-ol (XXXVIII) (500 mg.) gave androst-5-ene-3β : 17β-diol (XLI) (485 mg.), m. p. and mixed m. p. 177—180° (from ethyl acetate).

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63. *Phospholipids. Part IV.** myo*Inositol 2-Phosphate.*

By D. M. Brown and G. E. Hall.

The *myo*inositol monophosphates obtained from phytic acid by chemical hydrolysis and by use of wheat-bran enzyme cannot be distinguished from one another and are considered to be identical.

For comparative structural studies, as many as possible of the *myo*inositol phosphates are necessary. Iselin [1] synthesised a monophosphate, considered to be the 2-isomer, by phosphorylation of 1 : 3 : 4 : 5 : 6-penta-*O*-acetyl*myo*inositol. Monophosphates have also been obtained by chemical [2] and enzymic [3] hydrolysis of phytic acid (*myo*inositol hexaphosphate). On the basis of infrared spectra and *X*-ray powder diagrams Fleury, Desjobert, and Lecocq [4] concluded that the synthetically and enzymically prepared crystalline free acids were identical but different from that obtained by chemical hydrolysis of phytate. The three materials could not be differentiated in other respects.

We have prepared several samples of inositol monophosphate from phytic acid by the chemical and enzymic methods. Their infrared spectra and *X*-ray powder diagrams were identical, as were those of the derived bis*cyclo*hexylammonium salts. Specimens of barium inositol phosphate prepared chemically and enzymically were provided by Dr. Desjobert and converted into the crystalline free acids. Their spectra, and those of a sample of the synthetic inositol phosphate [1] prepared by Dr. Lecocq, were identical with those shown by our own products. We therefore confirm the identity of the synthetic and the enzymically prepared inositol phosphate and can find no evidence which differentiates these from that produced by chemical hydrolysis. Indeed we believe that the evidence allows the conclusion that all samples are identical.†

Experiments based on a personal communication from Dr. Lecocq were carried out, and these indicated that the abnormal spectra recorded [4] for the chemical-hydrolysis product are probably to be ascribed to a difference in crystalline form rather than to the existence of another isomer. In brief, crystallisation from water by addition of five volumes of alcohol gives a product with a different infrared spectrum and *X*-ray powder diagram. This " abnormal " product (which we were unable to obtain from the enzymically prepared acid) gives the usual *cyclo*hexylamine salt and it can also be converted into the normal acid by recrystallisation using ten volumes of ethanol. We avoid, in our own procedure, evaporation to dryness of aqueous solutions of the inositol phosphate to minimise the possibility of acid-catalysed phosphate migration. The isomer isolated is the predominant one present in the barium salts but, particularly in the salt from the enzymic hydrolysis, small amounts of other isomers are probably present.

Finally, there remains some doubt about the actual structure of the inositol phosphate under discussion. The synthetic route adopted by Iselin could only constitute proof of structure if acetyl migration in the intermediate penta-acetylinositol during phosphorylation were excluded. More recently, it has been shown [5] that Purdie methylation of the penta-acetate does involve acetyl migration, by the isolation of the (±)-1-methyl ether, DL-bornesitol, and that, where both the 1- and the 2-hydroxyl group are free, toluene-*p*-sulphonylation occurs on the 1-position.[6]

However, in the hydrolysis of phytic acid at pH values where phosphate migration

* Part III, *J.*, 1958, 1360.

† Dr. C. E. Ballou and Mrs. Frances Pizer (University of California, Berkeley) have informed us that they have reached the same conclusion.

[1] Iselin, *J. Amer. Chem. Soc.*, 1949, **71**, 3822.
[2] Desjobert, *Bull. Soc. Chim. biol.*, 1954, **36**, 1293.
[3] McCormick and Carter, *Biochem. Prep.*, 1952, **2**, 65.
[4] Fleury, Desjobert, and Lecocq, *Bull. Soc. Chim. biol.*, 1954, **36**, 1301.
[5] Anderson and Landel, *J. Amer. Chem. Soc.*, 1954, **76**, 6130.
[6] Angyal, *Quart. Rev.*, 1957, **11**, 212.

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cannot be important, five phosphate residues are removed more rapidly than the sixth, because the crude monophosphate is essentially one isomer. In *myo*inositol there is only one axial hydroxyl group so that, by analogy with carboxylic esters, the five equatorial phosphate groups should be hydrolysed most rapidly. The predominant monophosphate should then be the axial or 2-isomer. A similar view has been taken of the enzymic hydrolysis.[7] For this reason we intend to assume the correctness of Iselin's structural assignment until evidence to the contrary is forthcoming.

Experimental

myo*Inositol 2-Phosphate by Chemical Hydrolysis.*—Sodium phytate (200 g.) (or a solution prepared from the commercial calcium salt) was hydrolysed according to Desjobert's directions [2] and the product was isolated as the barium salt (17·6 g.) (Found, in material dried for 7 hr. at 60° *in vacuo*: C, 15·5; H, 3·7. Calc. for $C_6H_{11}O_9PBa,4H_2O$: C, 15·9 H, 4·1%). The barium salt (3·0 g.) was dissolved in water (50 c.c.) containing a few drops of formic acid, and the clear solution percolated through a column (13 × 3·3 cm.) of Dowex-50 (H^+-form) resin. The solution and washings were evaporated *in vacuo* to *ca.* 5 c.c., and ethanol (50 c.c.) was added; crystallisation began immediately. After 24 hr. at 0° the product was collected, washed with ethanol, then ether, and dried at room temperature [yield 1·42 g., 86%; m. p. 196—198° (decomp.)] (Found: C, 27·5; H, 5·25; P, 11·8. Calc. for $C_6H_{13}O_9P$: C, 27·7; H, 5·0; P, 11·9%). On recrystallisation from aqueous ethanol (1 : 10) the material had an unaltered infrared spectrum and *X*-ray powder diagram.

Hydrolysis with 3N-hydrochloric acid [1] gave *myo*inositol (75%), m. p. and mixed m. p. 226—230° (hexa-acetate, m. p. 222—223°).

*Bis*cyclo*hexylammonium* myo*Inositol 2-Phosphate.*—The above inositol phosphate (100 mg.) in water (5 c.c.) was added to *cyclo*hexylamine (0·2 c.c.), and the mixture extracted with ether (4 × 10 c.c.). The aqueous solution was evaporated *in vacuo* with exclusion of carbon dioxide. Addition of ethanol caused crystallisation, and the *salt* was recrystallised from methanol (10 c.c.) containing a few drops of water and ether (30 c.c.), giving rosettes of needles (125 mg., 62%), m. p. 211—213° (Found, in material dried *in vacuo* at 60° for 10 hr.: C, 40·4; H, 9·0; N, 5·4; P, 6·15. $C_{18}H_{39}O_9N_2P,4H_2O$ requires C, 40·7; H, 8·9; N, 5·3; P, 5·85%). No loss of *cyclo*hexylamine occurred at 100° in 9 hr. *in vacuo* (Found: N, 5·25%). The infrared spectrum showed bands at 3350, 2930, 2860, 2750, 2640, 2610, 2560, 2210, 2020, 1642, 1623, 1555, 1453, 1431, 1389, 1369, 1353, 1318, 1300, 1291, 1264, 1251, 1236 (shoulder), 1202, 1186, 1137, 1115, 1100 (shoulder), 1085 (shoulder), 1053, 1031, 1012, 968, 948, 924, 886, 822, and 728 $cm.^{-1}$. The *X*-ray powder photograph showed lines with $2l$ = 3·63, 4·33, 4·65, 5·12, 5·38, 5·73, 5·99, 6·25, 6·84, 7·16, 7·42, 8·30, 8·71, 9·00, 9·29, 9·56, 9·84, 10·27, and 10·88 cm.

cyclo*Hexylammonium* myo*Inositol Hydrogen Phosphate.*—The above di*cyclo*hexylammonium salt (247 mg.) and inositol phosphate (121 mg.) were dissolved in water, and the solution was evaporated. The residue was recrystallised from hot aqueous ethanol by the addition of ether to turbidity. The *product* formed needles (300 mg.), m. p. 203—205° (Found, in material dried for 6 hr. at 60°/1 mm.: C, 37·95; H, 7·7; N, 3·6. $C_{12}H_{26}O_9NP,H_2O$ requires C, 38·2; H, 7·5; N, 3·7%). Potentiometric titration with alkali gave an equivalent weight 377·5 (theor., 377).

Brucine myo*Inositol Hydrogen Phosphate.*—Brucine (1·0 g.) was warmed with a solution of inositol phosphate (260 mg.) in water (20 c.c.), and undissolved brucine removed. The solution was extracted 3 times with chloroform, and the aqueous layer evaporated under reduced pressure, ethanol being added towards the end to effect crystallisation. The product recrystallised from methanol (25 c.c.) containing a little water. The *salt* (536 mg.) had m. p. 244—247° (decomp.) (Found, in material dried for 4 hr. at 80°/1 mm. over P_2O_5: C, 51·05; H, 6·3; N, 4·1; P, 4·6. $C_{20}H_{39}O_{13}N_2P,1{\cdot}5H_2O$ requires C, 51·05; H, 6·2; N, 4·1; P, 4·55%).

myo*Inositol 2-Phosphate by Enzymic Hydrolysis.*—Sodium phytate (100 g.) was hydrolysed by the wheat-bran enzyme,[3] and the product (4·7 g.) was isolated, as above, as the barium rather than the lead salt. This barium salt (2·65 g.) was converted into the free acid as described for the chemical-hydrolysis product. Crystallisation was much slower and the

[7] Hawthorne, *Biochim. Biophys. Acta*, 1955, **18**, 389.

total yield less [1·0 g., 68%; m. p. 195—197° (decomp.)] (Found, in material dried at room temperature *in vacuo*: C, 27·8; H, 5·4%).

The acid (100 mg.) was converted into its bis*cyclo*hexylammonium salt as described above. This was recrystallised by dissolving in hot aqueous ethanol (1 : 1; 5 c.c.) and adding ether to turbidity and formed needles (150 mg., 74%), m. p. and mixed m. p. 210—212° (Found, in material dried at 60°/1 mm. for 3·5 hr.: C, 40·6; H, 9·1; N, 5·25%). The infrared spectrum and *X*-ray powder diagram were identical with those of the bis*cyclo*hexylamine salt of the inositol phosphate prepared by chemical hydrolysis.

Infrared and X-Ray Comparisons of Chemically and Enzymically Produced Inositol Phosphates.—Infrared spectra were obtained by using a Perkin-Elmer Model 21 with sodium chloride optics and Nujol and hexachlorobutadiene mulls. *X*-Ray powder diagrams were obtained by using a 19·0 cm. diameter camera and Cu-K_α radiation: the figures ($2l$) recorded are the distances between the two lines symmetrically disposed about the *X*-ray beam and corresponding to the same reflection, as measured on the film.

*myo*Inositol phosphate, prepared by either procedure, had infrared bands at 3340, 2910, 2300 (b), 1474, 1448, 1403, 1370, 1350 (shoulder), 1337, 1319, 1286, 1243, 1206, 1190 (shoulder), 1148, 1119, 1106, 1054, 1031, 990, 935, 819, 770 (b), and 712 cm.$^{-1}$, and lines on the *X*-ray powder photograph at $2l$ = 3·50, 5·03, 5·49, 5·80, 6·16, 6·54, 7·01, 7·35, 8·02, 8·33, 9·01, 9·30, 9·84, 10·20, 10·58, 10·88, 11·81, 12·29, 12·89, 13·50, and 13·86 cm. These spacings correspond closely to those reported by Fleury *et al.*[4] for the enzymic and the synthetic product.

These are described as type A spectra.

Samples of barium inositol phosphate kindly supplied by Dr. A. Desjobert and prepared from phytate chemically and enzymically were converted into the free acids as described above. A sample of synthetic *myo*inositol 2-phosphate prepared and kindly supplied by Dr. J. Lecocq was also studied. All gave type A infrared and *X*-ray spectra.

The following experiment based on information provided by Dr. Lecocq was carried out. Barium inositol phosphate (chemical hydrolysate) (0·97 g.) was shaken in water (55 c.c.) for 4 hr. Undissolved material (35 mg.) was filtered off, and barium removed by passage of the solution through a Dowex-50 (H^+-form) column. The solution was divided equally. The first part was evaporated to 5 c.c., and ethanol (25 c.c.) added. The inositol phosphate (184 mg.) (Found: C, 27·55; H, 5·4%) had spectra of type B, *viz.*, infrared bands at 3340, 2910, 2320 (b), 1470 (shoulder), 1448, 1401, 1382, 1371, 1335, 1315, 1284, 1265 (shoulder), 1240, 1203, 1146, 1117, 1105 (shoulder), 1050, 1033 (shoulder), 990, 935, 816, 785 (b), 718 (shoulder), and 710 cm.$^{-1}$.

The spacings on the *X*-ray powder diagram were similar to those given as type A, except that lines with $2l$ = 4·38, 8·64, and 13·01 appeared, whilst those with $2l$ = 6·54, 9·84, 12·29, and 12·39 cm. were absent. There were also intensity changes.

On recrystallisation (31 mg.) from aqueous ethanol (1 : 10) the product (26 mg., 84%) showed type A spectra. Preparation of the bis*cyclo*hexylammonium salt from unrecrystallised acid (type B spectra) (63 mg.) gave recrystallised material (67% yield) which had the same spectra as those recorded above for this salt.

The second part was taken to dryness *in vacuo*. The crystalline residue (240 mg.) had spectra of type A. This (158 mg.) was recrystallised by dissolving it in water (0·4 c.c.) and carefully adding ethanol (2·0 c.c.) to form a layer on top of the aqueous phase. After 60 hr. at room temperature, the large crystals (70 mg.) were filtered off, washed with aqueous ethanol (1 : 5), and dried *in vacuo*; the product gave spectra of type B. When this material (20 mg.) recrystallised from aqueous ethanol (1 : 10) at 0°, the product gave type A spectra.

This work was carried out during the tenure of a D.S.I.R. Award (by G. E. H.). We thank Sir Alexander Todd, F.R.S., for his interest, and Drs. Lecocq and Desjobert for their kindness in providing some inositol phosphate samples and for helpful personal communications. We are grateful to Ciba Laboratories Ltd., Horsham, for a generous gift of sodium phytate.

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64. *Reaction of Amino-derivatives of Anthraquinone, Fluorenone, and Fluorene with Nitrobenzene and α-Nitronaphthalene.*

By William Bradley and F. P. Williams.

Nitrobenzene and α-nitronaphthalene undergo nuclear substitution by arylamino-groups *para* to the nitro-substituent on being heated with potassium hydroxide and one or other of the amines, 1-amino-, 2-amino-, and 2-amino-1-chloro-anthraquinone and 2-aminofluorenone. Under similar conditions nitrobenzene and 2-aminofluorene give 2-aminofluorenone and 2-*p*-nitroanilinofluorenone.

Whilst several examples are known in which an amine in the form of an alkali-metal derivative replaces hydrogen in an aromatic nitro-compound very few instances have been described in which the same kind of reaction occurs with free amines. Thus nitrobenzene forms *N*-*p*-nitrophenylcarbazole [1] with potassiocarbazole, and α-nitronaphthalene gives 1-nitro-4-piperidinonaphthalene with sodamide and piperidine.[2] With 2-aminoanthraquinone however, nitrobenzene forms 2-*p*-nitroanilinoanthraquinone [3] when only potassium hydroxide is present and experiments have been undertaken to explore this type of reaction further.

Like the 2-amino-derivative 1-aminoanthraquinone reacts with nitrobenzene in the presence of potassium hydroxide, the product being 1-*p*-nitroanilinoanthraquinone identical with the compound prepared either from 1-chloroanthraquinone and *p*-nitroaniline or from 1-aminoanthraquinone and *p*-chloronitrobenzene. With α-nitronaphthalene 1-aminoanthraquinone gives 1-(4-nitro-1-naphthylamino)anthraquinone identical with the derivative prepared from 1-chloroanthraquinone and 4-nitro-1-naphthylamine or from 1-aminoanthraquinone and 1-chloro-4-nitronaphthalene. The reaction with α-nitronaphthalene occurs more readily than with nitrobenzene. Indanthrone is formed in small amount in the nitrobenzene reaction but none is found with α-nitronaphthalene, probably because of the greater ease of substitution into the naphthalene derivative. 2-Aminoanthraquinone similarly reacts more rapidly with α-nitronaphthalene than with nitrobenzene, the product being 2-(4-nitro-1-naphthylamino)anthraquinone identical with the product from 2-aminoanthraquinone and 1-chloro-4-nitronaphthalene. The ease with which substitution occurs in these cases can be gauged from the occurrence of analogous reactions with 2-amino-1-chloroanthraquinone. This derivative readily yields indanthrone by self-condensation in the presence of alkalis, but in nitrobenzene and pyridine the main product is 1-chloro-2-*p*-nitroanilinoanthraquinone. With α-nitronaphthalene 2-amino-1-chloroanthraquinone forms 1-chloro-2-(4-nitro-1-naphthylamino)anthraquinone.

2-Aminofluorenone with nitrobenzene forms 2-*p*-nitroanilinofluorenone identical with the derivative prepared from 2-aminofluorenone and *p*-chloronitrobenzene.

No reaction occurs between nitrobenzene and carbazole or piperidine unless the amines are used in the form of their alkali-metal derivatives. For this reason it is probable that 1-amino-, 2-amino-, and 2-amino-1-chloro-anthraquinone, as well as 2-aminofluorenone, participate in their reactions with nitrobenzene and α-nitronaphthalene after they have reacted with potassium hydroxide to form the corresponding anions.[4,5]

Experimental

Nitrobenzene and 1-Aminoanthraquinone.—1-Aminoanthraquinone (10 g.), powdered potassium hydroxide (6 g.), and dry nitrobenzene (80 c.c.) were stirred at 130—135° for 12 hr. The black suspension which was formed was mixed with alcohol (80 c.c.) and kept for a few hours,

[1] G. and M. de Montmollin, *Helv. Chim. Acta*, 1923, **6**, 94.
[2] Bradley and Robinson, *J.*, 1932, 1254.
[3] F.I.A.T. Final Report 1313, III, 82.
[4] Bradley and Leete, *J.*, 1951, 2129.
[5] Bradley and Nursten, *J.*, 1951, 2170.

then filtered. The residue (12·5 g.) was extracted with four portions of glacial acetic acid and the purple insoluble part (3·3 g.) was further extracted (Soxhlet) with chlorobenzene until nothing more dissolved. On being cooled the extract gave a reddish-brown solid which on being crystallised twice from pyridine gave needles of 1-*p*-nitroanilinoanthraquinone (1·7 g.), m. p. 302—303° (Found: C, 69·7; H, 3·5; N, 8·1. Calc. for $C_{20}H_{12}O_4N_2$: C, 69·8; H, 3·5; N, 8·1%). The acetic acid extracts gave mainly unchanged 1-aminoanthraquinone. The residue from the chlorobenzene extraction was blue; dissolution in concentrated sulphuric acid and addition to water gave indanthrone (0·15 g.), characterised by comparison of its chemical reactions and absorption spectrum with those of authentic material.

The above 1-*p*-nitroanilinoanthraquinone was identical with the product (Found: C, 69·7; H, 3·7; N, 8·3%) prepared from 1-aminoanthraquinone and *p*-chloronitrobenzene as described by Ullmann and Fodor,[6] who record m. p. 311°, and with that prepared from 1-chloroanthraquinone (10 g.), *p*-nitroaniline (6·6 g.), potassium carbonate (5·5 g.), copper bronze (0·2 g.), cupric acetate (0·5 g.), and nitrobenzene (50 c.c.) refluxed for 3 hr. After crystallisation from pyridine the resulting reddish-brown needles (6·5 g.), m. p. 302—303° (Found: C, 69·5; H, 3·5; N, 8·2%), dissolved in pyridine to form an orange solution which changed to red-violet on the addition of a drop of concentrated methanolic potassium hydroxide. The same reagent [4] added to an orange-yellow solution of 1-*o*-nitroanilinoanthraquinone gave a deep blue colour.

1-*Nitronaphthalene and* 1-*Aminoanthraquinone.*—(*a*) 1-Aminoanthraquinone (10 g.), finely powdered potassium hydroxide (10 g.), and 1-nitronaphthalene (8 g.) were stirred and heated for 12 hr. at 75—80° in dry pyridine (100 c.c.). The product was cooled, mixed with sodium-dried benzene (150 c.c.), and then stirred for 3 hr. at 50—60°. The black insoluble part was filtered off, and extracted with benzene (Soxhlet) until no more dissolved. The brown solid which remained was extracted with hot, dilute acetic acid and then crystallised twice from pyridine. Dark reddish-brown needles of 1-(4-*nitro*-1-*naphthylamino*)*anthraquinone* (1·8 g.), m. p. 335—336° (Found: C, 73·2; H, 3·3; N, 7·3. $C_{24}H_{14}O_4N_2$ requires C, 73·1; H, 3·6; N, 7·1%), separated. This derivative is slightly soluble in glacial acetic acid, more readily soluble in nitrobenzene, trichlorobenzene, and pyridine. It dissolves in concentrated sulphuric acid with a yellow-brown colour. The orange-yellow solution in pyridine changes to dark brown on the addition of methanolic potassium hydroxide.

(*b*) 1-Aminoanthraquinone (5 g.), 1-chloro-4-nitronaphthalene (5·5 g.), potassium carbonate (2·75 g.), cupric acetate (0·25 g.) and copper bronze (0·1 g.) were refluxed for 45 min. in nitrobenzene (30 c.c.). The solid was collected from the hot suspension, then extracted continuously with hot alcohol, and washed with dilute hydrochloric acid. The residue (5·5 g.) was crystallised twice from pyridine. The dark red-brown needles (4·2 g.) had m. p. 335—336°, not depressed by 1-(4-nitro-1-naphthylamino)anthraquinone prepared by method (*a*) (Found: C, 73·0; H, 3·4; N, 7·1%).

The same product was formed when 1-chloroanthraquinone (5 g.), 1-amino-4-nitronaphthalene (4·7 g.), potassium carbonate (2·75 g.), cupric acetate (0·25 g.), and copper bronze (0·1 g.) were refluxed in nitrobenzene (30 c.c.) for 3 hr. The product was crystallised from pyridine, and further purified by chromatography on alumina from trichlorobenzene (Found: C, 72·8; H, 3·5; N, 7·0%).

2-p-*Nitroanilinoanthraquinone.*—2-Aminoanthraquinone (10 g.), *p*-chloronitrobenzene (8 g.), potassium carbonate (5·5 g.), cupric acetate (0·5 g.), and copper bronze (0·2 g.) were refluxed in nitrobenzene (50 c.c.) for 1 hr. Crystallisation of the product from pyridine gave yellow-brown crystals (0·8 g.), m. p. 350—351°, not depressed by 2-*p*-nitroanilinoanthraquinone prepared from 2-aminoanthraquinone and nitrobenzene.

2-p-*Aminoanilinoanthraquinone.*—The 4-nitro-derivative (1 g.) was prepared in a finely divided state by dissolution in concentrated sulphuric acid (25 c.c.), addition to ice-water, and collection of the flocculent orange precipitate. After being washed until neutral the nitro-compound was heated with crystalline sodium sulphide (1 g.) in alcohol (200 c.c.); a dark red colour developed. Most of the alcohol was then removed by distillation and the residue was added to water. The resulting precipitate on being crystallised twice from chlorobenzene gave maroon needles, m. p. 294—296°, which were further purified by chromatography on alumina from a solution in chlorobenzene and elution with 95% alcohol. 2-p-*Aminoanilinoanthraquinone* has m. p. 296—297° (Found: C, 76·3; H, 4·7; N, 9·3. $C_{20}H_{14}O_2N_2$ requires C, 76·4; H, 4·5; N, 8·9%). It forms a pale bluish-green solution in concentrated sulphuric acid.

[6] Ullmann and Fodor, *Annalen*, 1911, **380**, 324.

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1-*Nitronaphthalene and* 2-*Aminoanthraquinone.*—(*a*) The 2-amino-quinone (8 g.) and potassium hydroxide (5 g.), both finely powdered, were shaken in a closed flask at the room temperature for 48 hr. with a solution of 1-nitronaphthalene (6·5 g.) in dry pyridine (125 c.c.). The dark green solid which was formed was mixed with chlorobenzene (250 c.c.) and stirred for 2 hr. at 50—60°. The undissolved black solid was collected (11·7 g.) and extracted, first with chlorobenzene and then with dilute acetic acid. Crystallisation from pyridine gave orange needles (3·6 g.) of 2-(4-*nitro*-1-*naphthylamino*)*anthraquinone*, m. p. 316—317° (Found: C, 73·0; H, 3·4; N, 7·1. $C_{24}H_{14}O_4N_2$ requires C, 73·1; H, 3·6; N, 7·1%). It dissolves sparingly in glacial acetic acid, more easily in trichlorobenzene, nitrobenzene, and pyridine. It gives a brown solution in concentrated sulphuric acid. Addition of methanolic potassium hydroxide to the orange solution in pyridine gives a deep purple colour. (*b*) The same compound, m. p. 316—317° (Found: C, 73·1; H, 3·5; N, 7·3%), resulted when 2-aminoanthraquinone (10 g.), potassium hydroxide (10 g.) and 1-nitronaphthalene (8 g.) were stirred and heated in pyridine (125 c.c.) for 8 hr. at 90—95° but the product prepared under these conditions was more difficult to purify. (*c*) It was also obtained (1·3 g.; m. p. 317—318°) (Found: C, 73·0; H, 3·6; N, 6·9%) when 2-aminoanthraquinone (10 g.) and potassium hydroxide (10 g.) were stirred for 4 hr. with molten 1-nitronaphthalene (75 g.) at 90°.

2-(4-Nitro-1-naphthylamino)anthraquinone was also prepared from 2-aminoanthraquinone (5 g.), 1-chloro-4-nitronaphthalene (5·5 g.), potassium carbonate (2·75 g.), copper acetate (0·25 g.), and copper (0·25 g.) refluxed in nitrobenzene (30 c.c.) for 1 hr. Crystallisation of the product from pyridine gave orange needles (0·9 g.) (Found: C, 73·4; H, 3·8; N, 7·3%), m. p. 316—317°, unchanged by admixture with the products obtained by methods (*a*), (*b*), and (*c*).

2-*Amino*-1-*chloroanthraquinone and Nitrobenzene.*—2-Amino-1-chloroanthraquinone (4 g.) and potassium hydroxide (4 g.) were stirred and heated with nitrobenzene (50 c.c.) at 50—60° for 12 hr. Chlorobenzene (100 c.c.) was then added and stirring was continued for 3 hr. The black suspension was cooled, kept overnight, and filtered, and the residue was washed with chlorobenzene and extracted exhaustively with benzene (Soxhlet). The undissolved portion was extracted with dilute acetic acid, and insoluble material (1·3 g.) was crystallised twice from pyridine. The resulting 1-*chloro*-2-p-*nitroanilinoanthraquinone* was obtained as orange needles, m. p. 343—345° (Found: C, 63·8; H, 2·8; N, 7·3; Cl, 9·4. $C_{20}H_{11}O_4N_2Cl$ requires C, 63·4; H, 2·9; N, 7·4; Cl, 9·4%). It dissolves in concentrated sulphuric acid with a deep blue colour (faint pink tinge); its orange-yellow solution in pyridine is changed to violet on the addition of methanolic potassium hydroxide.

Dehalogenation. On being heated with anhydrous potassium acetate (0·15 g.) and a small proportion of copper powder a solution of the above chloro-derivative (0·3 g.) in nitrobenzene (10 ml.) changed through dark green and reddish-brown to brown. The resulting solid was collected from the cooled suspension, washed with dilute hydrochloric acid, and crystallised from pyridine. The orange-brown needles, m. p. 352—354° (Found: C, 69·6; H, 3·4; N, 7·9. Calc. for $C_{20}H_{12}O_4N_2$: C, 69·8; H, 3·5; N, 8·1%), showed no depression of m. p. with authentic 2-*p*-nitroanilinoanthraquinone.

2-*Amino*-1-*chloroanthraquinone and* 1-*Nitronaphthalene.*—2-Amino-1-chloroanthraquinone (12 g.), potassium hydroxide (7·5 g.), and 1-nitronaphthalene (9 g.) were shaken in pyridine (100 c.c.) at the room temperature for 72 hr. The black product, treated as in the corresponding experiment with nitrobenzene and finally crystallised twice from pyridine, gave 1-*chloro*-2-(4-*nitro*-1-*naphthylamino*)*anthraquinone* (7·1 g.) as pale orange-yellow needles, m. p. 317—318° (Found: C, 67·5; H, 3·0; N, 6·4; Cl, 8·5. $C_{24}H_{13}O_4N_2Cl$ requires C, 67·2; H, 3·3; N, 6·5; Cl, 8·3%). It dissolves in concentrated sulphuric acid with a yellow-brown colour. The orange-yellow solution in pyridine is changed to violet on the addition of methanolic potassium hydroxide.

2-*Aminofluorenone and Nitrobenzene.*—2-Aminofluorenone [7] (10 g.) and potassium hydroxide (6 g.) were stirred for 5 hr. at 80—90° with nitrobenzene (100 c.c.). The black product which was formed was added to water, the resulting suspension was steam-distilled, and the residual dark brown solid was extracted with hot 3·5% hydrochloric acid. On being made alkaline the solution gave 2-aminofluorenone (3·2 g.). The acid-insoluble residue was extracted with toluene (Soxhlet). Crystals separated from the extract and these were recrystallised (2 g.) from toluene.

2-p-*Nitroanilinofluorenone* forms orange yellow prisms, m. p. 254—255° (Found: C, 72·3;

[7] Diels, *Ber.*, 1901, **34**, 1758.

H, 3·9; N, 8·9. $C_{19}H_{13}O_3N_3$ requires C, 72·2; H, 3·8; N, 8·9%). It dissolves in concentrated sulphuric acid with a violet colour. A deep purple colour develops on addition of methanolic potassium hydroxide to the yellow solution in pyridine.

2-*p*-Nitroanilinofluorenone was also prepared by refluxing 2-aminofluorenone (5 g.), *p*-chloronitrobenzene (4·8 g.), potassium carbonate (2·5 g.), cupric acetate (0·2 g.), and copper bronze (0·1 g.) in nitrobenzene (25 ml.) for 45 min. The product, m. p. 254—255° (Found: C, 72·0; H, 4·2; N, 8·6%), did not depress the m. p. of 2-*p*-nitroanilinofluorenone prepared by the previous method.

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65. *Synthesis in the Santonin Series. Part IV.* A Synthesis of the 7α(H)-3-Oxoeudesm-4-en-12-oic and 7β(H)-3-Oxoeudesm-4-en-12-oic Acids based on a Method of Oxidation of a Methylene to a Carboxyl Group.*

By R. HOWE, F. J. MCQUILLIN, and R. W. TEMPLE.

The sequence, $\rangle C{=}CH_2 \longrightarrow \rangle C(O)CH_2 \longrightarrow \rangle CH{\cdot}CHO \longrightarrow \rangle CH{\cdot}CO_2H$, has been developed as a method of oxidation of the terpenoid *iso*propenyl group, and has been applied to the synthesis of (−)-2-oxo-*p*-menthan-9-oic acid and of the two (+)-7α(H)-3-oxoeudesm-4-en-12-oic and two (+)-7β(H)-3-oxoeudesm-4-en-12-oic acids epimeric at $C_{(11)}$. The former pair have been related directly to the corresponding acids obtained by reduction of (−)-α- and (−)-β-santonin. A method is described for converting an acid from the 7β(H)- to the 7α(H)-series. Observations are reported on the preferential oxidation at an olefinic and a carboxyl group by respectively perbenzoic and monoperphthalic acid.

A METHOD of oxidation of a terpenoid *iso*propenyl substituent to a propionic acid residue as a synthetic route to 3-oxoeudesm-4-en-12-oic acids was described earlier.[1] Some of the stereochemical problems involved in this approach to santonin and related substances were resolved in the synthesis of (+)-α-cyperone.[2] Meantime also Abe *et al.*[3] fruitfully explored a different route to the synthesis of (±)-α-santonin which we also outlined.[4] To obtain the natural (−)-α- or (−)-β-isomers, however, this method involves optical resolution.[3] Our original approach continued therefore to be of interest as a method of interrelating optically active terpenes and as a potentially general method of carrying out the oxidation, $\rangle C{=}CH_2 \longrightarrow \rangle CH{\cdot}CO_2H$.

In our earlier experiments [1] oxidation of a terminal methylene to a carboxyl group was illustrated by the hydrogenolysis of (−)-dihydrocarvone 8 : 9-oxide (II), using Raney nickel, and oxidation of the derived diol (III) to (−)-2-oxo-*p*-menthan-9-oic acid (VIII). We later found it more convenient to hydrogenate (Raney nickel, pressure) (+)-carvone 8 : 9-oxide (VI) directly to the diol (III), though mild conditions (palladised barium carbonate) lead to the epoxy-dihydro-ketone (II). The same method has also been applied to (+)-limonene dioxide (X) which by hydrogenolysis and oxidation gives (+)-2-oxo-*p*-menthan-9-oic acid (XII), the enantiomorph of the previous acid [1] (VIII).

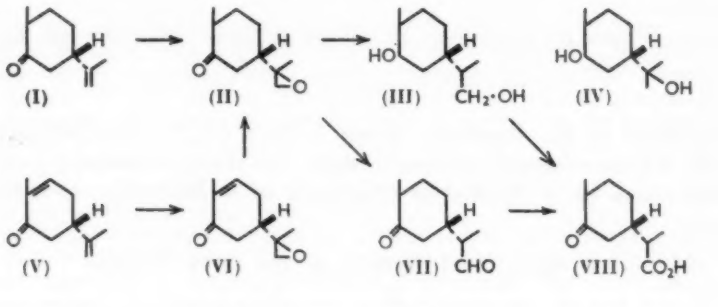
Hydrogenolysis of the epoxy-group in these instances is not, however, unidirectional. Newman, Underwood, and Renoll [5] give examples of fission of monoalkyl-substituted

* Part III, *J.*, 1953, 4060.

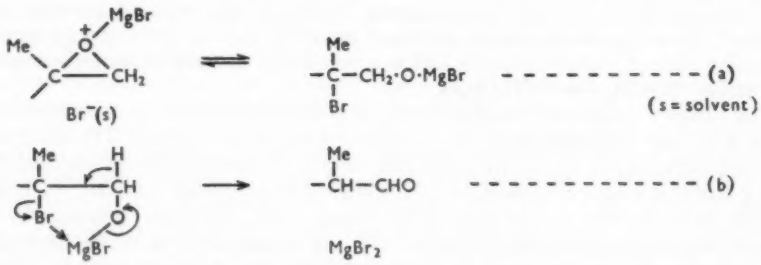
[1] Clemo and McQuillin, *J.*, 1952, 3839.
[2] McQuillin, *J.*, 1955, 528; Howe and McQuillin, *J.*, 1955, 2423.
[3] Abe, Harukawa, Ishikawa, Miki, Sumi, and Toga, *Proc. Jap. Acad.*, 1954, **30**, 116, 119.
[4] McQuillin, *Chem. and Ind.*, 1954, 311.
[5] Newman, Underwood, and Renoll, *J. Amer. Chem. Soc.*, 1949, **71**, 3362.

XUM

ethylene oxides at Raney nickel to the primary alcohol. In examples such as (II), (VI), or (X) the additional alkyl substituent will impede a nucleophilic reductive process at the tertiary centre. The diols obtained from hydrogenolysis contained material which was not oxidisable to the required acid and which we consider to be tertiary alcohols, *e.g.*, (IV); even under the mildest conditions material was also lost by complete removal of epoxy-oxygen; this has been noted in other instances.[6]



These results led us to examine as an alternative the known epoxy ⟶ oxo rearrangement induced by Lewis acids. In the initial experiments using magnesium bromide in ether,[7] made before the use of boron trifluoride [8] had become general, we obtained from (−)-dihydrocarvone oxide (II) a bromohydrin, or by removal of solvent and further heating the required (−)-aldehyde (VII). The oxide ⟶ bromohydrin sequence must be reversible by solvolysis (*a*). In absence of solvent intramolecular complex formation will replace solvation and provide the geometrical arrangement (*b*) necessary for rearrangement. The use of boron trifluoride–ether complex in benzene gave, however, a more convenient route to the aldehyde (VII) in good yield, and to the required acid (VIII).



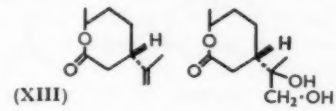
A point of interest arose in the preparation of dihydrocarvone oxide (II). Peracid may, in principle, react at the olefinic centre, or, by attack at the carbonyl group, lead to the

[6] Cf. Plattner, Petrzilka, and Lang, *Helv. Chim. Acta*, 1944, **27**, 513; Plattner, Furst, Koller, and Kuhn, *ibid.*, 1954, **37**, 258.

[7] Bedos, *Compt. rend.*, 1929, **189**, 255; Tiffeneau and Tchoubar, *ibid.*, 1938, **207**, 918, and later papers; Stoll and Commarmont, *Helv. Chim. Acta*, 1948, **31**, 1077; Bachmann, Horwitz, and Warzynski, *J. Amer. Chem. Soc.*, 1953, **75**, 3268; House, *ibid.*, 1955, **77**, 3070, 5083.

[8] Heusser, Eichenberger, Kurath, Dällenbach, and Jeger, *Helv. Chim. Acta*, 1951, **34**, 2106; Heusler and Wettstein, *ibid.*, 1953, **36**, 398; Bladon, Henbest, Jones, Lovell, Wood, Woods, Elks, Evans, Hathway, Oughton, and Thomas, *J.*, 1953, 2921.

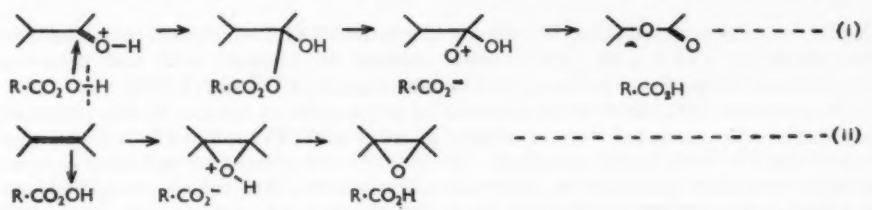
well-known ketone ⟶ lactone cleavage of the ring.[9] In the previous work,[1] using perbenzoic acid in chloroform, epoxidation was established as the main rapid reaction. Subsequently, monoperphthalic acid in ether was used with dihydrocarvone, and consumption of peracid was found extremely slow in a reaction leading to an unsaturated lactone as main product, and to the required oxide (II) in only small yield. The lactone, which on analogy [10] is regarded as (XIII), was characterised as a methyl ester, $[\alpha]_D$ +3·7°, which adsorbed one molecular equivalent of hydrogen on catalytic reduction. A corresponding lactone diol, $[\alpha]_D$ +71°, regarded as (XIV), was later isolated in small amount from the residues of oxidation of (−)-dihydrocarvone with perbenzoic acid in chloroform.



(XIII) (XIV)

The relatively slow epoxidation of olefins by monoperphthalic acid in ether is well known. Differential reactivity, in comparison with perbenzoic acid, favouring attack at a carbonyl group has not to our knowledge previously been noted. The ketone ⟶ lactone fission is known to be acid-catalysed; [11] the acid strength of phthalic (pK_a 3·0) in comparison with benzoic acid (pK_a 4·7), which will respectively be present as reaction products, may therefore be a factor; the peracids themselves are weak.[12] Consideration of the reaction sequences (i) and (ii) suggests, however, that the basicity of the solvent may be more important: monoperphthalic acid is commonly used in ether solution.

In the previous experiments,[1] (−)-2-oxo-*p*-menthan-9-oic acid (VIII) was used (as the methyl ester) in condensation with diethylmethyl-3-oxopentylammonium iodide to give a dextrorotatory product shown to have the structure of a 3-oxoeudesm-4-en-12-oic acid, the stereochemistry of which was not determined. Parallel work with (±)-methyl 2-oxo-*p*-menthan-9-oate was later described by Abe *et al.*[13] Alkylation of a 5-substituted 2-methyl*cyclo*hexanone in this way was, however, found by the Japanese authors, and shown also in other work [2,14] to lead to the undesired 7β(H)-eudesmane derivative as the

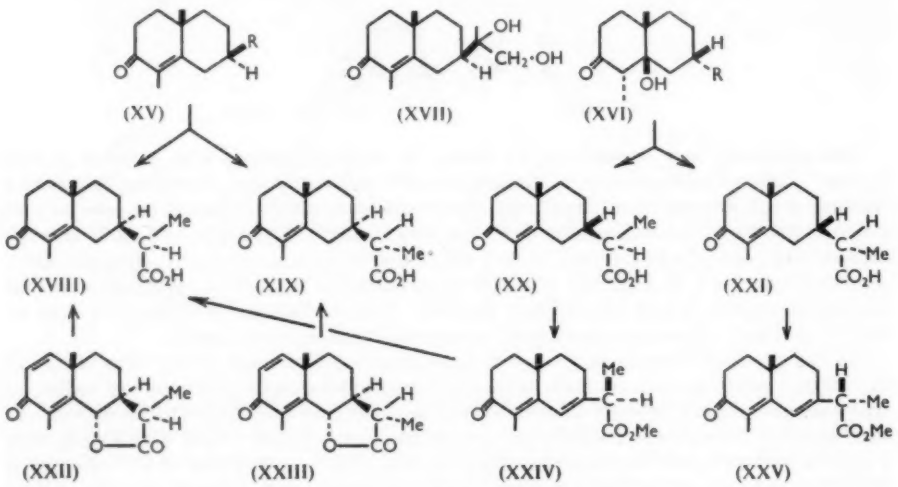


principal product. The oxidative sequence, oxide ⟶ aldehyde ⟶ acid, was therefore applied to (+)-α-cyperone (XVa), which we had previously synthesised,[2] and to the synthetic hydroxy-ketone [2,14] (XVIa) as sterically pure representatives of the 7α(H)- and 7β(H)-eudesmane series.

The required oxides (XVb) and (XVIb) were obtained in high yield by using perbenzoic acid in chloroform; in one experiment with insufficient cooling, (+)-α-cyperone gave largely the crystalline diol (XVII).

[9] Cf. Burckhardt and Reichstein, *Helv. Chim. Acta*, 1942, **25**, 821, 1434.
[10] Baeyer and Villiger, *Ber.*, 1899, **32**, 3625; cf. Murray, Johnson, Pederson, and Ott, *J. Amer. Chem. Soc.*, 1956, **78**, 981.
[11] Friess, *J. Amer. Chem. Soc.*, 1949, **71**, 2571; Doering and Speer, *ibid.*, 1950, **72**, 5515; Doering and Dorfmann, *ibid.*, 1953, **75**, 5595.
[12] Emmons and Pagano, *ibid.*, 1955, **77**, 89; Phillips, Frostick, and Starcher, *ibid.*, 1957, **79**, 5982.
[13] Abe, Harukawa, Ishikawa, Miki, Sumi, and Toga, *Proc. Jap. Acad.*, 1952, **28**, 425; *J. Amer. Chem. Soc.*, 1953, **75**, 2567.
[14] Howe and McQuillin, *J.*, 1958, 1194.

Henbest, Meakins, Nicholls, and Taylor [15] have drawn attention to a CH stretching frequency in the 3000 cm.$^{-1}$ region in the spectra of suitably substituted oxirans and in the present work we made a similar observation. The oxides (II), (XVb), and (XVIb), showed strong bands at 3034, 3016, and 3050 cm.$^{-1}$ respectively, and rearrangement of (+)-α-cyperone oxide (XVb) was conveniently followed by fall in absorption at 3016 cm.$^{-1}$ and development of the aldehyde band at 2700 cm.$^{-1}$ Treatment with a half-molar proportion of boron trifluoride–ether complex in benzene for 2 hr. gave a satisfactory result. A catalytic amount of boron trifluoride, on the other hand, rapidly converted the ketol oxide



(XV), (XVI); R = (*a*) $CMe{:}CH_2$, (*b*) $\overset{\frown O \frown}{CMe{\cdot}CH_2}$, (*c*) $CHMe{\cdot}CHO$, (*d*) $CHMe{\cdot}CO_2H$.

(XVIb) into the corresponding 11-epimeric aldehydes (XVIc) which were not separated. The aldehydes (XVc) and (XVIc) were oxidised by chromic acid and potassium permanganate respectively to the mixed 11-epimeric acids (XVd) and (XVId).

In agreement with the 5 : 10-*cis*-formulation of the hydroxy-ketone (XVIa), previously deduced on other grounds,[2,14] the crystalline hydroxy-acid (XVId) failed to lactonise when heated alone or with acetic anhydride. It could be dehydrated by refluxing aqueous-alcoholic potassium hydroxide, or, more conveniently with a little toluene-*p*-sulphonic acid in toluene. The 11-epimeric dehydro-acids were separated to give an acid, m. p. 121°, $[\alpha]_D$ +90°, from benzene–light petroleum, and a second acid which crystallised from dilute acetic acid as a monohydrate, m. p. 78°, $[\alpha]_D$ +208°. The former corresponds to the acid, m. p. 121°, $[\alpha]_D$ +91°, obtained by Abe *et al.*[16] by resolution of a (±)-synthetic acid and related by them to (+)-α-desmotroposantonin. In accord with the configuration for (−)-α-santonin deduced by Woodward and Yates,[17] our acid of m. p. 121° may be given the configuration (XXI). The hydrated acid, m. p. 78°, therefore has configuration (XX); a corresponding (±)-acid was described as having m. p. 125° (anhydrous) by Abe and his co-workers,[13] but it was not resolved.

From (+)-α-cyperone one of the corresponding pair of acids could readily be isolated, having m. p. 126°, $[\alpha]_D$ +126°, and after rigorous crystallisation was obtained with m. p.

[13] Henbest, Meakins, Nicholls, and Taylor, *J.*, 1957, 1459.
[16] Abe, Harukawa, Ishikawa, Miki, Sumi, and Toga, *J. Amer. Chem. Soc.*, 1956, **78**, 1416.
[17] Woodward and Yates, *Chem. and Ind.*, 1954, 1391; Corey, *J. Amer. Chem. Soc.*, 1955, **77**, 1044; Cocker and Edward, *Chem. and Ind.*, 1955, 41; cf., however, Abe, Miki, Sumi, and Toga, *ibid.*, 1956, 953; Cocker and McMurry, *ibid.*, 1956, 1430.

133°, $[\alpha]_D$ +130° (methyl ester, $[\alpha]_D$ +129°). The more soluble epimer was separated only with some difficulty and obtained having m. p. 105°, $[\alpha]_D$ +114° (methyl ester $[\alpha]_D$ +100°). Two corresponding racemic acids, m. p. 133° and 145°, described by Abe and his co-workers [3,18] were not resolved but were related respectively to the α- and the β-santonin series. We have directly related our (+)-synthetic acids, m. p. 133° and 105°, to (−)-α- and (−)-β-santonin respectively.

Bruderer, Arigoni, and Jeger,[19] in relating the stereochemistry of (−)-α-santonin to that of the cyperones, described the reduction of (−)-α-santonin (XXII) to an acid (XVIII), m. p. 124°, $[\alpha]_D$ +11·4° (methyl ester $[\alpha]_D$ +90°), by means of lithium in ammonia. We have repeated this preparation, and, through the kindness of Professor Jeger, we have been able to show that the acid, which we obtained having m. p. 126°, $[\alpha]_D$ +114° (methyl ester $[\alpha]_D$ +98°), gives an undepressed melting point with, and the same infrared spectrum as, the earlier Swiss preparation, also the same spectrum as our synthetic acid of m. p. 133°. This synthetic product may therefore be given the configuration (XVIII); it seems likely that the acid from reduction of (−)-α-santonin retains a small amount of a persistent lævorotatory impurity.

Reduction of (−)-β-santonin (XXIII) by lithium in ammonia led to an isomeric acid (XIX), m. p. 117°, $[\alpha]_D$ +111°. This showed characteristic differences in infrared absorption from the α-santonin acid (XVIII) and by this means separation of our synthetic acids could be followed. This separation was difficult; our purest preparation showed all the infrared bands characteristic of the β-santonin acid (XIX) and closely similar optical rotation, $[\alpha]_D$ +114°, but the melting point has not been raised beyond 105°. This second synthetic acid, however, clearly agrees closely with a structure (XIX).

The 7α(H)- and 7β(H)-series of 3-oxoeudesm-4-en-12-oic acids were interrelated by the method of partial reduction of a 4 : 6-dien-3-one applied earlier to (+)-β-cyperone.[20] The methyl ester of the acid (XX), m. p. 78°, $[\alpha]_D$ +208°, on bromination with *N*-bromosuccinimide and dehydrobromination with collidine (cf. Clemo and McQuillin [1]) gave a dienoic ester (XXIV). This, on half-hydrogenation in benzene with a modified Lindlar [21] catalyst and then hydrolysis, gave an acid, m. p. 123°, $[\alpha]_D$ +130°, identical in infrared absorption with the synthetic acid (XVIII) from (+)-α-cyperone, and different from the 7β(H)-acid (XXI), m. p. 121°, $[\alpha]_D$ +90°. This interconversion is in agreement with the configurations assigned and relates the two series of synthetic acids.

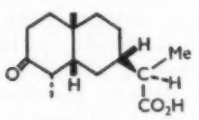
Complete hydrogenation of the dienoic ester (XXIV), $[\alpha]_D$ +392°, gave a tetrahydro-ester, $[\alpha]_D$ +23·7° which, however, is probably a mixture of 5α(H)- and 5β(H)-isomers. The isomeric acid (XXI), m. p. 121°, $[\alpha]_D$ +90°, gave a corresponding dienoic ester (XXV), $[\alpha]_D$ +201°, and a tetrahydro-derivative, $[\alpha]_D$ −12·6°.

A point of interest arose in connexion with the hydrogenation of the 7β(H)-eudesmenoic acids (XX) and (XXI). The former with palladised charcoal in alcohol gave a product, m. p. 126°, $[\alpha]_D$ +16·8°; the latter failed to absorb hydrogen and was recovered. The reduction product, m. p. 126°, is regarded as the *cis*-ring-fused acid (XXVI) which represents a stable configuration; *trans*-reduction will be strongly impeded by the 7α-substituent (cf. ref. 14). The non-reduction of the acid (XXI) is clearly related to the orientation of the carboxyl group, the bulk of which is known to impede catalytic reduction.[22]

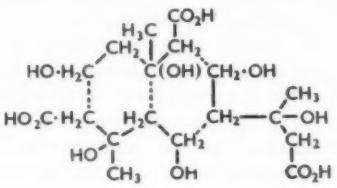
The oxidative sequence, $>C{=}CH_2 \longrightarrow$ oxide $\longrightarrow$ aldehyde $\longrightarrow$ acid, has analogy with, *e.g.*, the ozonolysis of longifolene to a C_{15} acid noted by Naffa and Ourisson [23] who record other examples. The mechanism may be similar. Our method was suggested by a

[18] Abe, Harukawa, Ishikawa, Miki, Sumi, and Toga, *J. Amer. Chem. Soc.*, 1956, **78**, 1422.
[19] Bruderer, Arigoni, and Jeger, *Helv. Chim. Acta*, 1956, **39**, 858.
[20] Howe and McQuillin, *J.*, 1956, 2670.
[21] Lindlar, *Helv. Chim. Acta*, 1952, **35**, 446.
[22] Cf. Dauben, Tweit, and MacLean, *J. Amer. Chem. Soc.*, 1955, **77**, 48; Wieland, Ueberwasser, Heusler, and Wettstein, *Helv. Chim. Acta*, 1958, **41**, 74.
[23] Naffa and Ourisson, *Bull. Soc. chim. France*, 1954, 1115.

biogenetic speculation [1] which regarded, for example, the various members of the eudesmane group as representing differing states of oxidation of a common precursor. The recognition that cholesterol [24] and also simpler terpenes [25] arise from acetate units *via* mevalonic acid lends point to this view. Reconsideration of the eudesmane series in these terms (XXVII) indicates that oxygenation at positions 3 and/or 12 probably does involve a subsequent oxidative step; the demethylation of lanosterol [24] and the origin of the carboxyl group of



(XXVI)



(XXVII)

eburicoic acid [26] are precedents. The 6α- and/or 8α-hydroxylation characteristic of the santonins and alantolactone,[27] on the other hand, may clearly arise from the mevalonic acid unit. The structure of pyrethrosin [28] also fits into this scheme and is interesting in relation to the oxygenation of *pseudo*santonin at position 1.

In naming the epimeric eudesmenoic acids (cf. Experimental section) the configuration at position 11 has been indicated by giving the 11-hydrogen substituent the appropriate α- or β-designation, with the convention that the formulæ are drawn as in (XVIII)—(XXI).

Experimental

$[\alpha]_D$ and $\lambda_{max.}$ values refer to solutions in chloroform and ethyl alcohol respectively. Infrared absorption was determined in liquid film (0·01 mm.) or, for solids, in a potassium bromide disc.

Oxidation of (−)-*Dihydrocarvone with Monoperphthalic Acid.*—(−)-Dihydrocarvone (20 g.) in ether (80 c.c.) was treated with monoperphthalic acid (24·5 g.) in ether (450 c.c.) at 0°. After 6 days the peracid was consumed and the product, isolated after washing with sodium hydrogen carbonate solution and water, gave recovered (−)-dihydrocarvone (4 g.) followed by material (7·5 g.), b. p. 105—116°/5 mm. The latter gave the semicarbazone of (−)-dihydrocarvone oxide, m. p. 188° (cf. Clemo and McQuillin [1]) in small yield. It was refractionated to give the *lactone*, b. p. 93—95°/2 mm., n_D^{20} 1·4735, of 6-hydroxy-3-*iso*propenylheptanoic acid (Found: C, 71·7; H, 9·9. $C_{10}H_{16}O_3$ requires C, 71·4; H, 9·5%). Hydrolysis by methanolic aqueous potassium hydroxide followed by esterification gave (+)-*methyl* 6-*hydroxy*-3-iso*propenylheptanoate*, b. p. 84—86°/0·2 mm., n_D^{20} 1·4595, $[\alpha]_D$ +3·7° (*c* 2·6) (Found: C, 66·1; H, 10·3. $C_{11}H_{20}O_3$ requires C, 66·0; H, 10·0%). Hydrogenated in alcohol over platinum the ester absorbed one mol. of hydrogen. Residues from oxidation of (−)-dihydrocarvone with perbenzoic deposited material of m. p. 103° (from benzene), $[\alpha]_D$ +71° (*c* 3·2) (Found: C, 59·8; H, 8·9. $C_{10}H_{18}O_4$ requires C, 59·5; H, 8·5%), regarded as the 6-*lactone* of 6-hydroxy-3-(1 : 2-dihydroxy-1-methylethyl)heptanoic acid.

(+)-2-*Oxo*-p-*menth*-6-*ene* 8 : 9-*Oxide.*—(+)-Carvone (23·5 g.) with perbenzoic acid (21 g.) in chloroform (400 c.c.) for 14 hr. at 20° gave (+)-2-oxo-*p*-menth-6-ene 8 : 9-oxide (VI) (21·4 g.), b. p. 128—132°/16 mm., $[\alpha]_D$ +37·6° (*c* 5·1) (Found: 71·9; H, 8·8. Calc. for $C_{10}H_{14}O_2$: C, 72·2; H, 8·4%). The *semicarbazone* formed prisms, m. p. 155°, from methanol (Found: C, 58·8; H, 8·0. $C_{11}H_{17}O_2N_3$ requires C, 59·2; H, 7·7%). Excess of reagent gave a *semicarbazidosemicarbazone*, m. p. 137° (from methanol) (Found: C, 48·2; H, 7·9. $C_{12}H_{22}O_3N_6$ requires C, 48·3; H, 7·4%). The 2 : 4-*dinitrophenylhydrazone*, m. p. 181° (from ethyl acetate), corresponded with a derivative of 2-oxo-*p*-menth-6-ene 8 : 9-diol (Found: C, 53·1; H, 5·6. $C_{16}H_{20}O_6N_4$ requires C, 52·8; H, 5·5%).

[24] Cf. Bloch, *Vitamins and Hormones*, 1957, **15**, 119.
[25] Birch, English, Massy-Westrop, and Smith, *J.*, 1958, 369.
[26] Dauben, Ban, and Richards, *J. Amer. Chem. Soc.*, 1957, **79**, 968.
[27] Tsuda, Tanabe, Iwai, and Funakoshi, *ibid.*, p. 5721.
[28] Barton and Mayo, *J.*, 1957, 150.

XUM

Hydrogenation of (+)-*Carvone Oxide*.—The oxide (5 g.) in ethanol (35 c.c.) with palladium–barium carbonate was reduced at 100 lb./sq. in. for 20 hr. to give (−)-dihydrocarvone oxide (3·4 g.), b. p. 108—110°/3 mm. (Found: C, 71·4; H, 9·8. Calc. for $C_{10}H_{16}O_2$: C, 71·4; H, 9·5%), identified as the semicarbazone, m. p. 187° (cf. Clemo and McQuillin [1]) (Found: C, 58·8; H, 8·7. Calc. for $C_{11}H_{19}O_2N_3$: C, 58·6; H, 8·4%).

(−)-α-(4-*Methyl*-3-*oxo*cyclo*hexyl*)*propionic Acid* (VIII).—(+)-Carvone oxide was hydrogenated at 80 atm. for various periods at 20° and at 80°. Brief reduction (~2 hr.) at 80° appeared to be optimal for production of *p*-menthane-2 : 9-diol, as estimated by the yield of acid on oxidation, but over-reduction to menthols could not be avoided. The diol fraction, oxidised as described by Clemo and McQuillin,[1] gave (−)-methyl α-(4-methyl-3-oxo*cyclo*hexyl)propionate, b. p. 78—81°/0·2 mm., n_D^{20} 1·4653, $[\alpha]_D$ −8·3° (*c* 2·8).

(+)-α-(4-*Methyl*-3-*oxo*cyclo*hexyl*)*propionic Acid* (XII).—(+)-Limonene dioxide (14 g.),[29] b. p. 115—118°/20 mm., $[\alpha]_D$ +49·5° (*c* 5·0), obtained in 85% yield by using perbenzoic acid in chloroform, was hydrogenated in ethanol (100 c.c.) at 90°/80 atm. with Raney nickel for 2·5 hr., to give 4·5 g. of material of b. p. 95—100°/0·2 mm., followed by *p*-menthane-2 : 9-diol (8 g.), b. p. 100—105°/0·2 mm. (Found: C, 69·9; H, 11·1. Calc. for $C_{10}H_{20}O_2$: C, 69·8; H, 11·6%). This diol was oxidised with potassium permanganate and the acidic product esterified to give (+)-*methyl* α-(4-*methyl*-3-*oxo*cyclo*hexyl*)*propionate*, b. p. 73—75°/0·2 mm., n_D^{20} 1·4616, $[\alpha]_D$ +10·9° (*c* 2·7) (Found: C, 66·5; H, 9·1. $C_{11}H_{18}O_3$ requires C, 66·7; H, 9·1%).

Rearrangement of (−)-*Dihydrocarvone Oxide*.—(i) *By magnesium bromide*. Mercuric bromide (21·6 g.) was added to a suspension of magnesium powder (3 g.) in dry ether (300 c.c.) and benzene (100 c.c.), and the mixture refluxed (2 hr.), filtered, and made up to 400 c.c. To this solution (320 c.c.), (−)-dihydrocarvone oxide (5 g.) was added in ether (30 c.c.) and the whole refluxed for 2·5 hr. Recovery gave a bromohydrin (3 g.), b. p. 123—125°/0·4 mm., n_D^{20} 1·5117, regarded as 2-*bromo*-2-(3-*oxo*-4-*methyl*cyclo*hexyl*)*propan*-1-*ol* (Found: C, 48·2; H, 7·0. $C_{10}H_{17}O_2Br$ requires C, 48·2; H, 6·8%). Alternatively the benzene and ether were removed by distillation and the residual magnesiobromo-complex heated on the water-bath for 1 hr. Recovery then gave (−)-α-(3-*oxo*-4-*methyl*cyclo*hexyl*)*propionaldehyde* (3·1 g.), b. p. 72—75°/0·2 mm., n_D^{20} 1·4765, $[\alpha]_D$ −22·3° (*c* 2·5) (Found: C, 71·7; H, 9·4. $C_{10}H_{16}O_2$ requires C, 71·4; H, 9·5%).

(ii) *By boron trifluoride*. (−)-Dihydrocarvone oxide (3 g.) in dry benzene (50 c.c.) with boron trifluoride–ether complex (2·5 g.) was kept for 0·5 hr. and then recovered, after treatment with sodium hydrogen carbonate solution, to give the aldehyde (VII) as above.

(−)-α-(3-*Oxo*-4-*methyl*cyclo*hexyl*)*propionic Acid* (VIII).—The foregoing aldehyde (0·8 g.), oxidised with the theoretical amount of potassium permanganate in water, gave the acid, isolated as the methyl ester (0·6 g.), b. p. 80°/0·1 mm., n_D^{20} 1·4638, $[\alpha]_D$ −13·3° (*c* 2·7) (Found: C, 66·3; H, 9·3. Calc. for $C_{11}H_{18}O_3$: C, 66·7; H, 9·1%) (2 : 4-dinitrophenylhydrazone, m. p. 169°) (cf. Clemo and McQuillin [1]).

11 : 12-*Epoxy*-5β-*hydroxy*-4β : 7β(H)-*eudesman*-3-*one* (XVIb).—(−)-5β-Hydroxy-4β : 7β(H)-eudesm-11-en-3-one (XVIa) (9·4 g.) in chloroform (50 c.c.) with perbenzoic acid (5·75 g.) in chloroform (115 c.c.) overnight at 0° gave (−)-11 : 12-*epoxy*-5β-*hydroxy*-4β : 7β(H)-*eudesman*-3-*one* (XVIb), m. p. 162°, $[\alpha]_D$ −51·3° (*c* 0·9), prisms (from benzene–light petroleum) (Found: C, 71·4; H, 9·6. $C_{15}H_{24}O_3$ requires C, 71·4; H, 9·5%).

(−)-5β-*Hydroxy*-3-*oxo*-4β : 7β(H)-*eudesman*-12-*al* (XVIc).—The epoxide above (5 g.) in dry benzene (250 c.c.) was treated with boron trifluoride–ether complex (0·5 g.) in benzene (25 c.c.) with stirring. After 8 min. 10% sodium hydrogen carbonate solution (50 c.c.) was added. The product isolated from the washed and dried benzene solution crystallised from benzene–light petroleum as prisms (4 g.), m. p. 126—127°, $[\alpha]_D$ −53·3° (*c* 1·3), of (−)-5β-*hydroxy*-3-*oxo*-4β : 7β(H)-*eudesman*-12-*al* (Found: C, 71·2; H, 9·7. $C_{15}H_{24}O_3$ requires C, 71·4; H, 9·5%).

(−)-5β-*Hydroxy*-3-*oxo*-4β : 7β(H)-*eudesman*-12-*oic Acid* (XVId).—The aldehyde above (6 g.) in acetone (60 c.c.) was treated with a solution of sodium carbonate (2·5 g.) in water (15 c.c.), followed by potassium permanganate (2·5 g.) in water (60 c.c.) with stirring during 1·5 hr. After a further 0·5 hr. the manganese dioxide was dissolved by means of sulphur dioxide, and organic material was isolated in chloroform. Extraction with sodium hydrogen carbonate solution and recovery of acidic material (5·2 g.) gave (−)-5β-*hydroxy*-3-*oxo*-4β : 7β(H)-*eudesman*-12-*oic acid* (XVId), m. p. 137—139° (from benzene–light petroleum), $[\alpha]_D$ −49·5° (*c* 0·9) (Found: C, 67·6; H, 9·3. $C_{15}H_{24}O_4$ requires C, 67·2; H, 9·0%).

[29] Prileshajew, *Ber.*, 1909, **42**, 4811.

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Dehydration of (−)-5β-*Hydroxy*-3-*oxo*-4β : 7β(H)-*eudesman*-12-*oic Acid*.—(i) The hydroxy-acid (0·5 g.) with 4% methanolic hydrogen chloride (25 c.c.), after refluxing, afforded the 11 epimeric methyl 3-oxo-7β(H)-eudesm-4-en-12-oates, b. p. 130—132°/0·1 mm., n_D^{20} 1·5145, $[\alpha]_D$ +109° (*c* 4·5) (Found: C, 72·5; H, 9·2. Calc. for $C_{16}H_{24}O_3$: C, 72·6; H, 9·1%) [2 : 4-dinitrophenylhydrazone, m. p. 167° (cf. Clemo and McQuillin [1]) (Found: C, 59·0; H, 6·3. Calc. for $C_{22}H_{28}O_6N_4$: C, 59·4; H, 6·3%)]. Hydrolysed by methanolic potassium hydroxide under nitrogen, this methyl ester afforded the mixed acids, $[\alpha]_D$ +131° (*c* 1·9). (ii) The hydroxy-acid (5 g.) in toluene (50 c.c.) with toluene-*p*-sulphonic acid (0·1 g.) was heated until the optical rotation had reached a maximum value. The recovered acid, $[\alpha]_D$ +140° (*c* 1·4), was chromatographed on silica gel and eluted with benzene–ether (20 : 1), to give (+)-3-*oxo*-7β : 11β(H)-*eudesm*-4-*en*-12-*oic acid* (XXI), m. p. 121—122°, $[\alpha]_D$ +90° (*c* 3·08), $\lambda_{max.}$ 250 mμ (log ε 4·13), after crystallisation from benzene–light petroleum (Found: C, 72·2; H, 9·0. $C_{15}H_{22}O_3$ requires C, 72·0; H, 8·8%). The *oxime*, m. p. 187—188°, $[\alpha]_D$ +61·2° (*c* 1·0 in EtOH), crystallised from aqueous methanol (Found: C, 67·6; H, 8·7. $C_{15}H_{23}O_3N_3$ requires C, 67·9; H, 8·7%). Diazomethane gave the *methyl ester*, b. p. 130°/0·1 mm., n_D^{20} 1·5156, $[\alpha]_D$ +57·4° (*c* 4·4), which crystallised as prisms, m. p. 47° (Found: C, 72·4; H, 9·1. $C_{16}H_{24}O_3$ requires C, 72·6; H, 9·1%). The remaining non-crystalline acid from chromatography was treated with dilute acetic acid and then gave (+)-3-*oxo*-7β : 11α(H)-*eudesm*-4-*en*-12-*oic acid monohydrate* (XX), prisms, m. p. 78°, $[\alpha]_D$ +208° (*c* 1·9), $\lambda_{max.}$ 251 mμ (log ε 4·17) (Found: C, 67·2; H, 9·2. $C_{15}H_{22}O_3,H_2O$ requires C, 67·2; H, 9·0%). The *methyl ester* formed an oil, b. p. 130°/0·1 mm., n_D^{20} 1·5185, $[\alpha]_D$ +176° (*c* 2·4) (Found: C, 72·6; H, 9·4%).

(+)-*Methyl* 3-*Oxo*-11β(H)-*eudesma*-4 : 6-*dien*-12-*oate* (XXV).—The methyl ester of the acid, m. p. 121° (XXI), was treated with *N*-bromosuccinimide in dry carbon tetrachloride under reflux for 1·5 hr., and the derived bromo-ester heated with *sym*-collidine on the steam-bath for 3·5 hr., to give (+)-*methyl* 3-*oxo*-11β(H)-*eudesma*-4 : 6-*dien*-12-*oate*, b. p. 120°/0·05 mm., n_D^{20} 1·5478, $[\alpha]_D$ +201·7° (*c* 3·15), $\lambda_{max.}$ 296 mμ (log ε 4·28) (Found: C, 72·8; H, 8·6. $C_{16}H_{22}O_3$ requires C, 73·3; H, 8·4%).

(+)-*Methyl* 3-*Oxo*-11α(H)-*eudesma*-4 : 6-*dien*-12-*oate* (XXIV).—The methyl ester of the acid, m. p. 78° (XX), treated similarly with *N*-bromosuccinimide followed by *sym*-collidine, afforded (+)-*methyl* 3-*oxo*-11α(H)-*eudesma*-4 : 6-*dien*-12-*oate*, b. p. 125°/0·1 mm., n_D^{20} 1·5503, $[\alpha]_D$ +392° (*c* 1·07), $\lambda_{max.}$ 298 mμ (log ε 4·27) (Found: C, 73·3; H, 8·7%).

Methyl 3-*Oxoeudesman*-12-*oates*.—(i) (+)-Methyl 3-oxo-11β(H)-eudesma-4 : 6-dien-12-oate (XXV), hydrogenated with palladised charcoal in alcohol, absorbed two mols. of hydrogen to give a methyl 3-oxoeudesman-12-oate, b. p. 120°/0·1 mm., n_D^{20} 1·4908, $[\alpha]_D$ −12·6° (*c* 4·43) (Found: C, 72·6; H, 10·0. $C_{16}H_{26}O_3$ requires C, 72·2; H, 9·8%). (ii) (+)-Methyl 3-oxo-11α(H)-eudesma-4 : 6-dien-12-oate (XXIV) similarly afforded a methyl 3-oxoeudesman-12-oate, b. p. 120°/0·1 mm., n_D^{20} 1·4928, $[\alpha]_D$ +23·7° (*c* 5·0) (Found: C, 72·6; H, 9·8%).

(+)-3-*Oxo*-7β(H)-*eudesman*-12-*oic acid* (XXVI).—The acid (XX), hydrogenated in alcohol with palladised charcoal, absorbed one mol. of hydrogen to give a product which was recrystallised from benzene–light petroleum and sublimed in *vacuo*, to give stout prisms, m. p. 126°, $[\alpha]_D$ +16·8° (*c* 1·64), regarded as 3-*oxo*-4β : 5β : 7β : 11α(H)-*eudesman*-12-*oic acid* (XXVI) (Found: C, 71·0; H, 9·4. $C_{15}H_{24}O_3$ requires C, 71·3; H, 9·5%).

(+)-11 : 12-*Epoxyeudesm*-4-*en*-3-*one* (XVb).—(+)-α-Cyperone (10·3 g.) in chloroform (150 c.c.) was treated at 2—3° with one equivalent of perbenzoic acid in chloroform (170 c.c.). Reaction was complete in 4·5 hr. The *epoxy-ketone*, isolated after washing of the solution with sodium hydrogen carbonate solution and with water, formed an oil (9 g.), b. p. 125°/0·3 mm., n_D^{20} 1·5238, $[\alpha]_D$ +108° (*c* 3·01) (Found: C, 76·6; H, 9·8. $C_{15}H_{22}O_2$ requires C, 76·9; H, 9·4%). After longer contact with the perbenzoic acid solution the epoxide was accompanied by (+)-11 : 12-*dihydroxyeudesm*-4-*en*-3-*one* (XVII), b. p. 130°/0·2 mm., m. p. 37° (from pentane), $[\alpha]_D$ +127·4° (*c* 2·6) (Found: C, 71·9; H, 9·2. $C_{15}H_{24}O_3$ requires C, 71·5; H, 9·5%).

(+)-*Eudesm*-4-*ene*-3 : 12-*dione* (XVc).—(+)-11 : 12-Epoxyeudesm-4-en-3-one (7·5 g.) in dry benzene (260 c.c.) was treated with boron trifluoride–ether complex (2·25 g.) and kept at the room temperature for 2·5 hr. The product, isolated after addition of sodium hydrogen carbonate solution and washing with water, formed an oil (5·5 g.), b. p. 129°/0·2 mm., n_D^{20} 1·5234, $[\alpha]_D$ +109° (*c* 2·13): it was (+)-*eudesm*-4-*ene*-3 : 12-*dione* (XVc) (Found: C, 77·0; H, 9·3. $C_{15}H_{22}O_2$ requires C, 76·9; H, 9·4%), and gave a bis-2 : 4-dinitrophenylhydrazone, m. p. 202° (Found: C, 55·0; H, 5·1. Calc. for $C_{27}H_{30}O_{8}N$: C, 54·5; H, 5·1%); Bruderer, Arigoni, and Jeger [19] give m. p. 203°.

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3-Oxoeudesm-4-en-12-oic Acids.—(+)-Eudesm-4-ene-3 : 12-dione (5 g.) in acetic acid (40 c.c.) with chromium trioxide (1·9 g.) in water (10 c.c.) was kept overnight. The acidic product (4 g.) largely crystallised. Repeated crystallisation first from benzene–light petroleum and finally from ether gave (+)-3-*oxo*-11α(H)-*eudesm*-4-*en*-12-*oic acid* (XVIII), m. p. 133—134°, $[\alpha]_D$ +130° (*c* 1·03), $\lambda_{max.}$ 250 mμ (log ε 4·2) (Found: C, 71·8; H, 9·2. $C_{15}H_{22}O_3$ requires C, 72·0; H, 8·8%) [*methyl ester*, b. p. 125°/0·1 mm., n_D^{20} 1·5132, $[\alpha]_D$ +129° (*c* 0·72) (Found: C, 72·9; H, 9·3. $C_{16}H_{24}O_3$ requires C, 72·8; H, 9·1%)]. From the remaining material by means of benzene–light petroleum an acid, m. p. 95°, was obtained. Chromatography on silica gel and elution with benzene–ether (20 : 1) failed to raise the m. p. as did repeated crystallisation from benzene–light petroleum or ethyl acetate–light petroleum. Exhaustive recrystallisation from aqueous methanol removed a little of the acid (XVIII) in the less soluble fractions and finally yielded, from the more soluble, prisms, m. p. 105°, $[\alpha]_D$ +114° (*c* 1·7), $\lambda_{max.}$ 250 mμ (log ε 4·2), regarded as (+)-3-*oxo*-11β(H)-*eudesm*-4-*en*-12-*oic acid* (XIX) (Found: C, 71·7; H, 8·8. $C_{15}H_{22}O_3$ requires C, 72·0; H, 8·8%); it gave a *methyl ester*, b. p. 125—130°/0·1 mm., n_D^{20} 1·5108, $[\alpha]_D$ +100° (Found: C, 73·1; H, 9·0. $C_{16}H_{24}O_3$ requires C, 72·8; H, 9·1%), and a *semicarbazone*, m. p. 210° (Found: C, 62·5; H, 8·2. $C_{16}H_{25}O_3N_3$ requires C, 62·5; H, 8·1%).

Lithium–Ammonia Reduction of (−)-α- *and* (−)-β-*Santonin.*—(i) Reduction of (−)-α-santonin carried out essentially as described by Bruderer, Arigoni, and Jeger [19] gave directly an acid product which largely crystallised, and gave (+)-3-oxo-11α(H)-eudesm-4-en-12-oic acid, m. p. 126° (after crystallisation from benzene–light petroleum and sublimation *in vacuo*), $[\alpha]_D$ +114° (*c* 3·34), $\lambda_{max.}$ 250 mμ (log ε 4·1) (Found: C, 72·4; H, 8·8. Calc. for $C_{15}H_{22}O_3$: C, 72·0; H, 8·8%) {*methyl ester*, b. p. 120°/0·05 mm., n_D^{20} 1·5102, $[\alpha]_D$ +98·5° (*c* 4·5) (Found: C, 72·5; H, 9·2. Calc. for $C_{16}H_{24}O_3$: C, 72·8; H, 9·1%)}. (ii) (−)-β-Santonin (1 g.) in tetrahydrofuran (50 c.c.) was added to a solution of lithium (0·3 g.) in liquid ammonia (200 c.c.) with stirring and the liquid kept for 24 hr.; the ammonia had then evaporated. Acidic material (0·8 g.) was purified *via* the methyl ester which was chromatographed and hydrolysed, to give (+)-3-oxo-11β(H)-eudesm-4-en-12-oic acid, m. p. 117° (after recrystallisation from ether–light petroleum and sublimation *in vacuo*), $[\alpha]_D$ +110·5° (*c* 3·24), $\lambda_{max.}$ 250 mμ (log ε 4·15) (Found: C, 72·2; H, 8·6. Calc. for $C_{15}H_{22}O_3$: C, 72·0; H, 8·8%) {*methyl ester*, b. p. 130°/0·1 mm., n_D^{20} 1·5132 $[\alpha]_D$ +96° (*c* 1·4) (Found: C, 72·7; H, 9·4. $C_{16}H_{24}O_3$ requires C, 72·8; H, 9·1%)}.

Inversion of (+)-3-*Oxo*-7β : 11α(H)-*eudesm*-4-*en*-12-*oic Acid* (XX) *to* (+)-3-*Oxo*-7α : 11α(H)-*eudesm*-4-*en*-12-*oic Acid* (XVIII).—Methyl 3-oxo-11β(H)-eudesma-4 : 6-dien-12-oate (XXIV) (1·8 g.) in benzene (25 c.c.) in presence of palladium–strontium carbonate which had been treated with lead acetate (Howe and McQuillin [14]) absorbed 1 mol. of hydrogen. Recovery gave a methyl ester (1·7 g.), b. p. 130°/0·1 mm., $\lambda_{max.}$ 247 (log ε 3·98) and 296 mμ (log ε 3·56), which was hydrolysed by methanolic potassium hydroxide. The acid was heated at 130°/0·1 mm., to decarboxylate residual dienone-carboxylic acid, and acidic material (1·1 g.) was then recovered and converted into the *oxime*. This formed prisms, m. p. 185° (from methanol), $[\alpha]_{5461}$ +86·7° (*c* 0·6 in EtOH), $\lambda_{max.}$ 243 mμ (log ε 4·25) (Found: C, 67·4; H, 9·0. $C_{15}H_{23}O_3N$ requires C, 67·9; H, 8·7%). The oxime was boiled in aqueous-methanolic hydrochloric acid for 4 hr., giving an acidic product (0·35 g.) which on trituration with ether–light petroleum gave (+)-3-oxo-11α(H)-eudesm-4-en-12-oic acid, m. p. 123°, $[\alpha]_D$ +126° (*c* 2·8), $\lambda_{max.}$ 250 mμ (log ε 4·14) (Found: C, 71·7; H, 9·2. Calc. for $C_{15}H_{22}O_3$: C, 72·0; H, 8·8%). The mixed m. p. with authentic acid (XVIII) was 123°.

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66. *Ammonolysis and Aminolysis of Trifluoromethyl Arsenicals.*

By W. R. Cullen and H. J. Emeléus.

Chlorobistrifluoromethylarsine reacted with ammonia and amines. The new arsenicals, $(CF_3)_2As{\cdot}NH_2$, $[(CF_3)_2As]_2NH$, $(CF_3)_2As{\cdot}NHR$ (R = Me or Et), and $(CF_3)_2As{\cdot}NMe_2$, were characterised. Tristrifluoromethylarsine also reacted with ammonia and amines, as did tristrifluoromethylstibine.

Arsenic trihalides react with ammonia in the liquid or the gas phase and form initially the triamide, which loses ammonia above 0° to give ill-defined solid imides.[1,2] The ammonolysis and aminolysis of organo-arsenic compounds has been incompletely investigated, though chlorodiphenylarsine and ammonia are known to form aminodiphenylarsine.[3,4] It has been shown [5] that chlorobistrifluoromethylphosphine and ammonia give the stable compound aminobistrifluoromethylphosphine and, in this paper, a number of analogous reactions of trifluoromethyl arsenicals are described.

Chlorobistrifluoromethylarsine reacted readily with liquid ammonia at low temperatures to give perfluorocacodylamine, $[(CF_3)_2As]_2NH$, but with liquid ammonia at room temperature all the trifluoromethyl groups were liberated slowly as fluoroform. In the gas phase, however, both perfluorocacodylamine and aminobistrifluoromethylarsine resulted. Chlorodimethylarsine and ammonia were shown in preliminary experiments to give only solid products. Dichlorophenylarsine and dichloromethylarsine both form solids of the type $(RAs{=}NH)_x$, where R = Me or Ph.[3] The reaction of dichlorotrifluoromethylarsine with ammonia likewise gave solid products, but fluoroform was also liberated. Its formation was almost quantitative with liquid ammonia at room temperature and this is a major point of difference between the alkyl and the trifluoromethyl arsenicals.

The reaction of chlorobistrifluoromethylarsine with primary and secondary amines in the gas phase gives the aminoarsines in good yield:

$$(CF_3)_2AsCl + 2HNRR' = (CF_3)_2As{\cdot}NRR' + RR'NH,HCl$$

The methylamino-, ethylamino-, and dimethylamino-compounds were made in this way, the results being analogous to those of Harris.[5] Only in the case of chlorobistrifluoromethylarsine and aniline was the reaction more complex. This is being further studied.

Fully alkylated or arylated compounds of the elements of Groups III—VI are stable to ammonia [1] and, in order to cleave the M–C bond it is necessary to add a catalyst such as sodium [6] or potassamide.[7] Ammonia and amines, however, solvolyse most organometallic derivatives of Groups I and II: for example, ammonia and diethylzinc give ethane and zinc amide,[8] while aniline and diphenylmagnesium form dianilinomagnesium and benzene.[9] There was no reaction between tristrifluoromethylarsine and ammonia in the gas phase but, with liquid ammonia at 20°, solvolysis was complete. Tristrifluoromethylstibine also reacted with liquid ammonia and the end-product was probably antimony nitride, as it is when antimony trihalides are subject to ammonolysis.[1] With the trifluoromethylarsine, reaction is slower than with arsenic trihalides, and the intermediates aminobistrifluoromethylarsine and diperfluorocacodylamine can be isolated if excess of ammonia is avoided or the reaction is carried out below room temperature. The rate of ammonolysis of the compounds $(CF_3)_3M$ (M = P, As, or Sb) appears to increase in the order P < As <

[1] Fernelius and Bowman, *Chem. Rev.*, 1940, **26**, 3.
[2] Besson, *Compt. rend.*, 1890, **110**, 1258; Hugot, *ibid.*, 1904, **139**, 54.
[3] Ipatiew, Rasuwajew, and Stromski, *Ber.*, 1929, **62**, 598.
[4] Banks, Morgan, Clark, Hatlelid, Kahler, Paxton, Cragoe, Andres, Elpern, Coles, Lawhead, and Hamilton, *J. Amer. Chem. Soc.*, 1947, **69**, 927; Doak, *J. Amer. Pharm. Assoc.*, 1935, **24**, 453.
[5] Harris, *J.*, 1958, 512.
[6] Kraus and Sessions, *J. Amer. Chem. Soc.*, 1925, **47**, 2361.
[7] Hauser and Hance, *ibid.*, 1951, **73**, 5846.
[8] Fitzgerald, *ibid.*, 1907, **29**, 656.
[9] Schlenk, *Ber.*, 1931, **64**, 736.

Sb and this order is also found for alkaline hydrolysis.[10] Alkaline hydrolysis of tetrakistrifluoromethyldiarsine yielded[11] fluoroform (84%) and fluoride (16%), but ammonolysis of the diarsine gave at least 88% of the trifluoromethyl as fluoroform and no fluoride.

Tristrifluoromethylarsine reacted with aliphatic amines, but not with aniline, with evolution of fluoroform, but only in the case of dimethylamine was the expected aminoarsine, dimethylaminobistrifluoromethylarsine, formed. It is likely, however, that ethyltrifluoromethylamine, $CF_3{\cdot}NHEt$, was formed in the reaction of the arsine with ethylamine. Tristrifluoromethylstibine was extensively aminolysed by dimethylamine.

The aminotrifluoromethylarsines were colourless liquids. Dimethylaminobistrifluoromethylarsine reacted readily with water, yielding fluoroform, dimethylamine, and arsenious acid. Cyanobistrifluoromethylarsine reacts similarly with water.[11] The dimethylamino-compound was stable to oxygen but, with hydrogen chloride, gave chlorobistrifluoromethylarsine and dimethylammonium chloride. It was stable at 160° above its boiling point, whereas the monomethylamino-compound decomposed at less than 40° above its boiling point: in both cases fluoroform was the main volatile product. It would be expected that hydrogen atoms attached to nitrogen atoms in these compounds would be acidic because of the strong inductive effect of the trifluoromethyl groups. Methylaminobistrifluoromethylarsine did not, however, react with sodium at 50°, and the only evidence of acid character was a gradual increase in conductivity of a solution of tristrifluoromethylarsine in ammonia at −64°. This may be due to partial ammonolysis, followed by ionisation to $[(CF_3)_2AsNH]^-$ and NH_4^+.[12]

Experimental

Trifluoroiodomethane and the trifluoromethyl arsenicals were prepared by recorded methods.[11,13] All were tensimetrically pure and the techniques used were similar to those previously described.

Reaction of Chlorobistrifluoromethylarsine with Ammonia.—Chlorobistrifluoromethylarsine (1·705 g.) and dry ammonia (0·53 g.) were allowed to react at −64° (45 min.), and the products were separated by repeated fractional condensation in traps cooled to 0°, −23°, and −46°. The main product, condensed at −23°, was *diperfluorocacodylamine*, $[(CF_3)_2As]_2NH$ (Found: C, 10·8; H, 0·26; N, 3·4%; *M*, 439. $C_4HNF_{12}As_2$ requires C, 10·9; H, 0·23; N, 3·4%; *M*, 441). Vapour pressures (84—125°) were given by $\log_{10} p(\text{mm.}) = 7{\cdot}974 - 2030/T$. The b. p. was 126·5° ± 0·5°, the latent heat of vaporisation 9300 cal./mole, and Trouton's constant 23·3.

Chlorobistrifluoromethylarsine (0·913 g.) and ammonia (0·127 g.) were allowed to react in the gas phase by introducing the two gases into 500 ml. bulbs connected by a wide-bore tap. The products separated were impure diperfluorocacodylamine (0·425 g.; *M*, 380), which showed the same infrared spectrum as the material above, and a fraction, condensed at −78° (0·140 g.), which had the infrared spectrum of aminobistrifluoromethylarsine (Found: *M*, 275. $C_2H_2NF_6As$ requires *M*, 229). The latter arsine was best prepared by the ammonolysis of tristrifluoromethylarsine (see below). With excess of ammonia (1 g.) at 20° (5 days) chlorobistrifluoromethylarsine (0·312 g.) was completely ammonolysed to fluoroform (0·175 g. Found: *M*, 79·0).

Reaction of Chlorobistrifluoromethylarsine with Methylamine.—Chlorobistrifluoromethylarsine (0·571 g.) and methylamine (0·162 g.) reacted immediately in the gas phase at 20°, forming a mixture which on fractionation gave *methylaminobistrifluoromethylarsine* (0·510 g., 92%) (Found: C, 15·0; H, 1·8; N, 5·9%; *M*, 244. $C_3H_4NF_6As$ requires C, 14·8; H, 1·6; N, 5·8%; *M*, 243). The vapour pressure (20—82°) was given by $\log_{10} p(\text{mm.}) = 7{\cdot}986 - 1825/T$. The b. p. was 84° ± 0·5°, the latent heat of vaporisation 8360 cal./mole, and Trouton's constant 23·4. Methylaminobistrifluoromethylarsine (0·260 g.) did not react with sodium at 50°. A sample (0·588 g.) heated at 120° for 15 hr. gave fluoroform (0·180 g.), tristrifluoromethylarsine

[10] Haszeldine and West, *J.*, 1957, 3880.
[11] Emeléus, Haszeldine, and Walaschewski, *J.*, 1953, 1552.
[12] Cullen, Ph.D. Thesis, Cambridge, 1958.
[13] Haszeldine, *J.*, 1951, 584; Brandt, Emeléus, and Haszeldine, *J.*, 1952, 2552; Walaschewski, *Ber.*, 1953, **86**, 272.

XUM

(0·07 g.) (Found: *M*, 257. Calc. for C_3F_9As: *M*, 282), identified by the infrared spectrum, and a black solid which after treatment with water contained 3% of carbon and showed the *X*-ray powder photograph of elementary arsenic.

Reaction of Chlorobistrifluoromethylarsine with Ethylamine.—Chlorobistrifluoromethylarsine (0·297 g.) and ethylamine (0·110 g.) in the gas phase gave *ethylaminobistrifluoromethylarsine* (0·240 g., 78%) (Found: C, 18·9; H, 2·2; N, 5·6%; *M*, 258. $C_4H_6NF_6As$ requires C, 18·7; H, 2·3; N, 5·5%; *M*, 257). Vapour pressures (19—95°) were given by $\log_{10} p(\text{mm.}) = 7{\cdot}609 - 1711/T$. The b. p. was 98·5° ± 0·5°, the latent heat of vaporisation 8520 cal./mole, and Trouton's constant 23·0.

Reaction of Chlorobistrifluoromethylarsine with Dimethylamine.—Chlorobistrifluoromethylarsine (0·855 g.) and dimethylamine (0·318 g.) in the gas phase gave *dimethylaminobistrifluoromethylarsine* (0·728 g., 80%) (Found: C, 18·8; H, 2·6; N, 5·6%; *M*, 259. $C_4H_6NF_6As$ requires C, 18·7; H, 2·3; N, 5·4%; *M*, 257). Vapour pressures (23—85°) were given by $\log_{10} p(\text{mm.}) = 7{\cdot}868 - 1858/T$. The b. p. was 89° ± 0·5°, the latent heat of vaporisation 7840 cal./mole, and Trouton's constant 21·7. Dimethylaminobistrifluoromethylarsine did not react with oxygen at 20° (7 days; 96% recovery of arsenical). The arsenical (0·264 g.) and hydrogen chloride (0·062 g.) reacted immediately at room temperature, forming a white solid and chlorobistrifluoromethylarsine (0·160 g.), identified by its infrared spectrum. The solid was dimethylammonium chloride (m. p. 166°; lit.,[14] 171°). Dimethylaminobistrifluoromethylarsine (0·311 g.) when heated in a Carius tube was stable to 250° but decomposed at 250—280°, giving fluoroform (0·065 g.) and a black solid. The solid was attacked by water to give a water-insoluble residue which contained elemental arsenic. The arsenical was hydrolysed by water to fluoroform, dimethylamine, and arsenious acid.

Reaction of Tristrifluoromethylarsine with Ammonia.—The vapours of tristrifluoromethylarsine and ammonia did not react at 20° (2 hr.). Reaction of the arsenical (0·566 g.) and ammonia (0·150 g.) at −64° gave *aminobistrifluoromethylarsine* (0·2 g.) (Found: C, 10·6; H, 0·5; N, 6·3%; *M*, 229. $C_2H_2NF_6As$ requires C, 10·5; H, 0·9; N, 6·1%; *M*, 229). Vapour pressures (40—85°) were given by $\log_{10} p(\text{mm.}) = 7{\cdot}470 - 1662/T$. The b. p. was 89° ± 1°, the latent heat of vaporisation 7610 cal./mole, and Trouton's constant 21·0. Fluoroform (0·063 g.) was also formed (Found: *M*, 69·5. Calc. for CHF_3: *M*, 70). Tristrifluoromethylarsine (1·584 g.) and ammonia (*ca.* 1 g.) in a Carius tube (1 week) gave fluoroform (1·084 g.), equivalent to 92% of the trifluoromethyl present. In an experiment with 2 g. of ammonia the yield was 97%. Reaction of the arsenical (3·029 g.) and ammonia (0·293 g.) at 20° for 2 days gave fluoroform (0·33 g.), diperfluorocacodylamine (0·34 g.) (Found: *M*, 410. Calc. for $C_4HNF_{12}As_2$: *M*, 441), and aminobistrifluoromethylarsine (0·228 g.) (Found: *M*, 227. Calc. for $C_2H_2NF_6As$: *M*, 229). The arsine (6·130 g.) and ammonia (0·170 g.) did not react at −78° in 4 days. At 20° in 7 days fluoroform (0·047 g.) was produced and ammonia (0·161 g.) was recovered.

Aminolysis of Tristrifluoromethylarsine.—Tristrifluoromethylarsine (0·670 g.) and methylamine (0·240 g.) at 20° in 7 days gave fluoroform (0·20 g.; *M*, 70·5). Tristrifluoromethylarsine (1·038 g.) and a large excess of ethylamine in a Carius tube in 1 week gave fluoroform (0·31 g.), equivalent to 40% of the trifluoromethyl present. At least two solid phases were produced in addition to a volatile fraction which condensed in a trap at −64° and was possibly *ethyltrifluoromethylamine*, v. p. 65 mm. at 20° (Found: C, 32·1; H, 5·3; N, 12·8%; *M*, 113—115. $C_3H_6NF_3$ requires C, 31·9; H, 5·7; N, 12·5%; *M*, 113). The fraction was strongly adsorbed by tap grease and decomposed to a brown-red solid when left in a glass tube at 20°. It was not formed when the arsine (2·067 g.) and ethylamine (2 g.) were kept together at 20° for 28 days. There was no reaction between tristrifluoromethylarsine (0·680 g.) and aniline (2 g.) at 20° in 14 days.

Reaction of Dichlorotrifluoromethylarsine with Ammonia.—Dichlorotrifluoromethylarsine (0·521 g.) and ammonia (0·169 g.) in a Carius tube at 20° in 8 days gave fluoroform (0·113 g.; *M*, 71·0), equivalent to 66% of the trifluoromethyl present. With a large excess of ammonia, in a second experiment, 90% of the trifluoromethyl was liberated as fluoroform in 4 days at 20°.

Ammonolysis and Aminolysis of Tristrifluoromethylstibine.—The stibine (0·424 g.) and ammonia (1 g.) in a Carius tube in 24 hr. gave fluoroform (0·265 g.; *M*, 70·5) equivalent to 98% of the trifluoromethyl present. A yellow solid was also formed which was probably mainly antimony nitride (Found: N, 10·95. Calc. for SbN: N, 10·3%). Tristrifluoromethylstibine

[14] Delépine, *Ann. Chim.* (*France*), 1896, **8**, 439.

XUM

(1·137 g.) and dimethylamine (4·0 g.) reacted at 20° in 28 days, to give fluoroform (0·663 g.; *M*, 70·3) equivalent to 91% of the trifluoromethyl present.

Reaction of Tristrifluoromethylphosphine with Ammonia.—The phosphine (0·229 g.) and ammonia (1 g.) at 20° in 48 hr. gave fluoroform (0·074 g.; *M*, 70·4) equivalent to 37% of the trifluoromethyl present. No solid phase was produced.

Reaction of Tetrakistrifluoromethyldiarsine with Ammonia.—The diarsine (0·244 g.) and ammonia (1·5 g.) reacted at low temperature in a Carius tube, to give a green solution and a white precipitate which slowly became red-brown. The colour gradually faded from the liquid layer and after 28 days at 20° 89% of the trifluoromethyl was liberated as fluoroform (0·143 g.; *M*, 70·5). No fluoride was produced.

Reaction of Chlorodimethylarsine with Ammonia and Dimethylamine.—The arsine (0·551 g.) and ammonia (0·5 g.) reacted in a cold finger in the liquid phase at −46°, giving solid products. Fractionation failed to isolate any unchanged arsine. No part of the solid was soluble in benzene or ether. Chlorodimethylarsine and dimethylamine gave a fraction which condensed at −64° and had an infrared spectrum consistent with that expected from dimethylaminodimethylarsine. The fraction was decomposed by tap grease.

Infrared Spectra.—The spectra were measured on a Perkin-Elmer Model 21 Spectrometer with rock-salt optics and were obtained from liquid films. The results were as follows (the letters have their usual meaning).

$(CF_3)_2As{\cdot}NH_2$: 3430w, 3350m, 2240w, 1840vw, 1630vw, 1567w, 1552w, 1450vw, 1264m, 1172vs, 1146vs, 945vw, 896w, 805s, 728s.

$[(CF_3)_2As]_2NH$: 3360m, 2920vw, 2240w, 1840vw, 1645vw, 1440vw, 1264m, 1175vs, 1124vs, 805s, 728s.

$(CF_3)_2As{\cdot}NHMe$: 3375w, 2920w, 2820w, 2210w, 1580vw, 1483w, 1463w, 1473w, 1370vw, 1260w, 1174vs, 1122vs, 1073vs, 757w, 725w.

$(CF_3)_2As{\cdot}NHEt$: 3375m, 2975s, 2885m, 2220w, 1648vw, 1563vw, 1475w, 1456m, 1391m, 1348w, 1322w, 1260m, 1172vs, 1120vs, 1067vs, 910w, 803w, 755w, 724m.

$(CF_3)_2As{\cdot}NMe_2$: 2910s, 2870m, 2820m, 2220w, 1640w, 1470m, 1457m, 1448m, 1262m, 1174vs, 1123vs, 1075vs, 955w, 775m, 724m.

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67. *The Heptafluoropropyliodophosphines and their Derivatives.*

By H. J. Emeléus and J. D. Smith.

Reaction of heptafluoroiodopropane with phosphorus at 200—220° gave bisheptafluoropropyliodophosphine and heptafluoropropyldi-iodophosphine. No trisheptafluoropropylphosphine was found. The two iodo-compounds afforded various derivatives and were less readily hydrolysed than their trifluoromethyl analogues. Heptafluoropropylphosphonous, heptafluoropropylphosphonic, and bisheptafluoropropylphosphinic acid were prepared: all were strong acids. Preliminary experiments on the reaction of heptafluoroiodopropane with arsenic are also described.

Trifluoromethyl compounds of phosphorus are readily prepared by interaction of trifluoroiodomethane and phosphorus at 195—250°.[1] The products, tristrifluoromethylphosphine, iodobistrifluoromethylphosphine, and di-iodotrifluoromethylphosphine, are formed at 230° in the rough proportions 7 : 2 : 1, and increasing temperature favours formation of the tris-compound. The iodine in the two iodo-compounds may readily be replaced by other groups and hydrolysis yields trifluoromethylphosphonous acid,[2] which

[1] Bennett, Emeléus, and Haszeldine, *J.*, 1953, 1565.
[2] *Idem*, *J.*, 1954, 3598.

XUM

can be oxidised to the corresponding phosphonic acid. In the experiments described below the analogous reaction of heptafluoroiodopropane with phosphorus has been studied, to determine the influence of the larger heptafluoropropyl group on the initial reaction and on the properties of a number of derivatives of the products.

Reaction of heptafluoropropyliodopropane with phosphorus began at about 200° and was conveniently carried out at 220—230°. Surprisingly, no trisheptafluoropropylphosphine was isolated but only a mixture of bisheptafluoropropyliodophosphine and heptafluoropropyldi-iodophosphine. This result was obtained even when the conditions should, by analogy with the behaviour of trifluoroiodomethane, have favoured production of the tris-compound. Vapour-phase chromatography was used in attempts to detect the presence of the trisheptafluoropropyl compound.

Tripropylphosphine may be made from the trichloride by the Grignard reaction [3] and the same method has been used for butylphosphines.[4] Trisheptafluoropropylphosphine may, therefore, be accessible by reaction of phosphorus trichloride with heptafluoropropyllithium [5] or heptafluoropropylmagnesium iodide.[6]

Preliminary experiments on the reaction of heptafluoroiodopropane with arsenic showed that, although reaction occurs readily at 200—220° with formation of heptafluoropropyl arsenicals, fluorocarbons are formed simultaneously and prevent the separation and characterisation of the desired products. These fluorocarbons are probably the result of the breakdown of the arsenicals, rather than of decomposition of heptafluoroiodopropane, since they are formed to only a minor extent in the reaction of heptafluoroiodopropane with sulphur at 300—400°.[7] Tristrifluoromethylarsine and trispentafluoroethylarsine decompose at a conveniently measurable rate at 350—410° and 270—310°, respectively,[8] and it is therefore likely that the heptafluoropropyl derivatives would show incipient instability at 200—300°, which, if it led to liberation of radicals such as C_3F_7, would produce fluorocarbons.

The two heptafluoropropyliodophosphines reacted readily with silver chloride to form the corresponding chloro-compounds. Chlorobisheptafluoropropylphosphine added chlorine and formed trichlorobisheptafluoropropylphosphorane, $(C_3F_7)_2PCl_3$, which decomposed at 125° to a complex mixture which included chloroheptafluoropropane, dichloroheptafluoropropylphosphine, and chlorobisheptafluoropropylphosphine. The chief difference between the heptafluoropropyl compounds and their trifluoromethyl analogues, apart from volatility, was in the slower hydrolysis of the former. For example, ethyl bisheptafluoropropylphosphinite was incompletely decomposed by water, even at 150°, whereas the corresponding trifluoromethyl compound, prepared by the interaction of chlorobistrifluoromethylphosphine with alcohol, was hydrolysed at room temperature with quantitative liberation of fluoroform. Similarly, aminobisheptafluoropropylphosphine was only partially hydrolysed at room temperature, whereas aminobistrifluoromethylphosphine was readily decomposed.[9]

Chlorobisheptafluoropropylphosphine also reacted with ammonia to form aminobisheptafluoropropylphosphine, $(C_3F_7)_2P{\cdot}NH_2$ and with ethyl alcohol to form ethyl bisheptafluoropropylphosphinite, $(C_3F_7)_2P{\cdot}OEt$. Alkaline hydrolysis of these compounds resulted in quantitative liberation of heptafluoropropane. Both heptafluoropropyliodo-compounds gave heptafluoropropylphosphonous acid, $C_3F_7{\cdot}PO{\cdot}OH$, with water with elimination of one molecule of heptafluoropropane in the case of the monoiodo-compound. The acid was isolated in a pure state (b. p. 71°/0·7 mm.) by hydrolysis of dichloroheptafluoropropylphosphine. The titration curve showed it to be a strong and monobasic acid. It

[3] Davies, Pearse, and Jones, *J.*, 1929, 1262.
[4] Davies and Jones, *J.*, 1929, **33**.
[5] Pierce, McBee, and Judd, *J. Amer. Chem. Soc.*, 1954, **76**, 474.
[6] McBee, Pierce, and Meiners, *ibid.*, 1953, **75**, 2516.
[7] Haszeldine and Kidd, *J.*, 1955, 3871.
[8] Ayscough and Emeléus, *J.*, 1954, 3381.
[9] Harris, *J.*, 1958, 512.

was oxidised in aqueous solution by iodine and also reduced mercuric to mercurous chloride at 60°. When the aqueous solution was oxidised by hydrogen peroxide, heptafluoropropylphosphonic acid was formed. This was isolated as white deliquescent needles of the dihydrate. The titration curve was similar to that of trifluoromethylphosphonic acid, the slightness of the first inflection indicating a small ratio of the two dissociation constants, as is found for oxalic and malonic acids. Mean values of the dissociation constants calculated by Britton's method[10] were $1{\cdot}3 \times 10^{-1}$ and $1{\cdot}1 \times 10^{-4}$, the corresponding values of pK_1 and pK_2 being 0·9 and 3·96. Heptafluoropropylphosphonic acid was stable to hydrolysis by excess of alkali. Bisheptafluoropropylphosphinic acid was prepared from trichlorobisheptafluoropropylphosphorane by adding the stoicheiometric amount of water. It was a white deliquescent solid, the titration curve of which was typical of a strong, monobasic acid. At room temperature excess of sodium hydroxide liberated 1 mol. of heptafluoropropane. The acid sublimed without decomposition in a vacuum at 66—68°.

When the conductivities of the two monobasic acids were measured in water at 25° the plots of equivalent conductivity against the square root of molar concentration were linear at low concentrations, extrapolation to zero concentration giving values of the equivalent conductivities at infinite dilution of 367 ohm^{-1} $cm.^2$ for $(C_3F_7)_2PO{\cdot}OH$ and 363 ohm^{-1} $cm.^2$ for $C_3F_7{\cdot}PHO{\cdot}OH$.[11] The derived equivalent conductivities of the bisheptafluoropropylphosphinate and heptafluoropropylphosphonite ions are $17{\cdot}5 \pm 1{\cdot}5$ and $12{\cdot}9 \pm 1{\cdot}5$ ohm^{-1} $cm.^2$. For heptafluoropropylphosphonic acid the plot of equivalent conductivity against square root of concentration is not a straight line. The same is true of trifluoromethylphosphonic acid,[12] as well as sulphuric,[13] malonic, and oxalic acid. For none of these acids can the equivalent conductivity at infinite dilution be determined. A rough comparison between the acidity of these heptafluoropropyl oxyacids of phosphorus and the acidity of sulphuric and perchloric acids was made with a limited range of Hammett indicators.[14] It was shown that the acidity of saturated solutions of bisheptafluoropropylphosphinic and heptafluoropropylphosphonic acid, and of liquid heptafluoropropylphosphonous acid (H_0 = approx. −6 to −8) was appreciably greater than that of 70% perchloric acid (H_0 = approx. −5·5) but less than that of 98% sulphuric acid (H_0 = approx. −9). These high acidities are associated with the presence in the molecule of the electronegative heptafluoropropyl group. It is not possible, however, to decide from the data whether these acids are stronger or weaker than their trifluoromethyl analogues.

The ultraviolet absorption spectra of the heptafluoropropyliodophosphines and their derivatives show the same general features as those of the trifluoromethyl derivatives, with the expected small shift of the absorption maxima to longer wavelengths.[15] The infrared spectra show the pattern of C–F stretching frequencies and CF_3 and CF_2 angle deformation frequencies which seem to be characteristic of all compounds containing the n-C_3F_7 group.[16] The detailed shape of the absorption pattern between 1000 and 1350 $cm.^{-1}$ allows compounds with one C_3F_7 group to be distinguished from those with two C_3F_7 groups. The spectrum of aminobisheptafluoropropylphosphine shows N–H stretching frequencies at 3480 and 3390 $cm.^{-1}$, and the NH_2 angle deformation frequency at 1567 $cm.^{-1}$. In the spectra of ethyl bistrifluoromethylphosphinite and ethyl bisheptafluoropropylphosphinite, C–H stretching frequencies appear between 2860 and 3000 $cm.^{-1}$, and the frequencies characteristic of the OEt system between 1360 and 1500 $cm.^{-1}$. The frequencies at 1039 and 937 $cm.^{-1}$ in the spectrum of $(CF_3)_2P{\cdot}OEt$ and at 1026 and 945 $cm.^{-1}$ in the spectrum of $(C_3F_7)_2P{\cdot}OEt$ are assigned to the P–O–Et group and in each case the first frequency is

[10] Britton, "Hydrogen Ions," Chapman and Hall, 1955, Vol. I, p. 218.
[11] For data *see* J. D. Smith, Ph.D. Thesis, Cambridge, 1958.
[12] Emeléus, Haszeldine, and Paul, *J.*, 1955, 563.
[13] Sherrill and Noyes, *J. Amer. Chem. Soc.*, 1926, **48**, 1861.
[14] Long and Paul, *Chem. Rev.*, 1957, **57**, 1.
[15] Haszeldine, *J.*, 1953, 1764.
[16] Hauptschein and Grosse, *J. Amer. Chem. Soc.*, 1951, **73**, 2461.

within the narrow range (1050—980 cm.$^{-1}$) for characteristic P–O–Et absorption. The spectra of the heptafluoropropylphosphorus oxyacid derivatives are similar to those of the trifluoromethyl compounds and have been useful for characterising these materials.

Experimental

Preparation of Heptafluoroiodopropane.—Heptafluoroiodopropane (b. p. 40—41°) was made in 90% yield by heating dry silver heptafluorobutyrate with iodine.[16] The product decomposed slowly in light, forming iodine and perfluorohexane.

Reaction of Heptafluoroiodopropane with Red Phosphorus.—Red phosphorus was washed with sodium hydroxide solution and water and dried (P_2O_5). Purified phosphorus (25 g.) was placed in a 300 ml. stainless-steel autoclave, heptafluoroiodopropane (*ca.* 50 g.) was introduced *in vacuo* and the autoclave was filled with dry nitrogen before being sealed. In 8 hr., little reaction occurred at 200°, but at 220—230° about 60% of the heptafluoroiodopropane was converted into phosphorus derivatives. These were pumped from the autoclave *in vacuo* and condensed at −46°. They contained about 70% of bisheptafluoropropyliodophosphine, the balance being heptafluoropropyldi-iodophosphine. The proportion of the latter increased with the reaction time at 235°. *Bisheptafluoropropyliodophosphine* and *heptafluoropropyldi-iodophosphine* were separated with difficulty by trap-to-trap fractional condensation: the former condensed at −23° (Found: C, 14·9; C_3F_7, 67·7; I, 25·5. $C_6F_{14}IP$ requires C, 14·5; C_3F_7, 68·1; I, 25·6%) and the latter at −3° (Found: C, 8·1; C_3F_7, 35·0; I, 54·8; P, 6·6. $C_3F_7I_2P$ requires C, 7·9; C_3F_7, 37·2; I, 55·9; P, 6·8%). The former was a pale yellow liquid, the vapour pressure of which (at 0—80°) was given by $\log_{10} p(\text{mm.}) = 8{\cdot}096 - 2170/T$. The extrapolated b. p. was 135°, the latent heat of evaporation 9920 cal./mole, Trouton's constant 23·7, and the m. p. −108°. Only slight decomposition and disproportionation occurred during the vapour-pressure measurements, which were made with a spiral pressure gauge used as a null instrument. The compound reacted with mercury, giving a colourless liquid, probably tetrakisheptafluoropropyldiphosphine. The monoiodo-compound was rapidly and quantitatively decomposed by aqueous alkali, all the fluorine being liberated as heptafluoropropane. This reaction was used in analysis. Bisheptfluoropropyliodophosphine (0·329 g., 0·663 mmole) and water (4 ml.), when sealed in a Carius tube for 4 days, gave heptafluoropropane (0·112 g., 0·660 mmole) (Found: *M*, 169. Calc. for C_3HF_7: *M*, 170). When the remaining volatile material was heated at 100° for 48 hr. a further 0·0997 g. (0·592 mmole) of heptafluoropropane was formed, equivalent to almost complete decomposition of the heptafluoropropylphosphonous acid formed in the aqueous hydrolysis at room temperature. Hydrolysis by 2N-hydrochloric acid gave a similar result, half of the heptafluoropropane being liberated at room temperature and half at 120°.

Heptafluorodi-iodopropylphosphine was a yellow liquid, the vapour pressure of which (at 40—120°) was given by $\log_{10} p(\text{mm.}) = 7{\cdot}350 - 2070/T$. The extrapolated b. p. was 190° ± 2°, the latent heat of evaporation 9470 cal./mole, Trouton's constant 20·5, and the m. p. −18°. There was appreciable decomposition during the vapour-pressure determination at the higher temperatures. The compound was decomposed by aqueous alkali, and all of the fluorine was liberated as heptafluoropropane.

No trisheptafluoropropylphosphine was isolated even after reaction at 300°, which favours formation of tristrifluoromethylphosphine from trifluoroiodomethane and phosphorus. Then the product from the autoclave reaction (3·46 g.) was treated with silver chloride to convert the two iodo-compounds into chloro-derivatives, and next with α-naphthylamine (1 g.) in pentane, and there was no volatile product. Since both chloro-compounds react with α-naphthylamine and, by analogy with tristrifluoromethylphosphine, the trisheptafluoropropyl compound would not, this experiment strongly supports the absence of the latter.

Since the two iodotrifluoromethylphosphines are known to disproportionate to products which include tristrifluoromethylphosphine, the disproportionation of the heptafluoroiodophosphines was studied with a Perkin–Elmer vapour-phase fractometer. Purified bisheptafluoropropyliodophosphine and heptafluoropropyldi-iodophosphine, when passed through the column, had retention times of 2·3—2·5 and 13·3—13·8 min. That of heptafluoroiodopropane was 1·1—1·2 min. By estimating the areas under the peaks in the record it was shown that a pure sample of the monoiodo-compound when heated at 220° in a Carius tube (48 hr.) gave unchanged material (75%), di-iodo-compound (2%), and heptafluoroiodopropane (16%). The di-iodo-compound when heated similarly gave unchanged material (18%), monoiodo-compound

(36%), and heptafluoroiodopropane (46%). Phosphorus tri-iodide was also produced in the disproportionation but was not introduced into the column. In neither case was there a peak attributable to trisheptafluoropropylphosphine. Bennett *et al.*[1] showed that a considerable amount of tristrifluoromethylphosphine was formed on disproportionation under similar conditions.

Derivatives of the Heptafluoropropyliodophosphines.—(a) *Chlorobisheptafluoropropylphosphine.* Bisheptafluoropropyliodophosphine (11·6 g.), sealed in a Carius tube with silver chloride (35 g.) for 11 days, gave *chlorobisheptafluoropropylphosphine* (8·95 g., 96%) (Found: C, 17·7; Cl, 8·6; C_3F_7, 83·2; P, 7·5%; *M*, 397. $C_6ClF_{14}P$ requires C, 17·8; Cl, 8·8; C_3F_7, 83·5; P, 7·7%; *M*, 404). It was a colourless liquid; vapour pressures (at 10—100°) were given by $\log_{10} p$(mm.) = 7·883 − 1956/*T*. The b. p. was 118—119°, the latent heat of evaporation 8970 cal./mole, Trouton's constant 22·9, and the m. p. −75°. Hydrolysis by excess of 20% sodium hydroxide solution was rapid and quantitative at room temperature. Chlorobisheptafluoropropylphosphine (0·270 g., 0·669 mmole), sealed with water (4 ml.) for 4 days at 20°, gave heptafluoropropane (0·114 g., 0·672 mmole) (Found: *M*, 168. Calc. for C_3HF_7: *M*, 170).

(b) *Dichloroheptafluoropropylphosphine.* Heptafluoropropyldi-iodophosphine (4·09 g.), similarly treated with silver chloride, gave *dichloroheptafluoropropylphosphine* (2·39 g., 98%) (Found: Cl, 26·0; C_3F_7, 62·7; P, 11·9%; *M*, 272. $C_3Cl_2F_7P$ requires Cl, 26·2; C_3F_7, 62·5; P, 11·4%; *M*, 271). Vapour pressures (at 0—75°) were given by $\log_{10} p$(mm.) = 7·744 − 1748/*T*. The b. p. was 86·4° ± 1°, the latent heat of evaporation 8000 cal./mole, Trouton's constant 22·3, and the m. p. −90°. This and the preceding compound disproportionated less readily than the iodo-analogues.

(c) *Trichlorobisheptafluoropropylphosphorane.* Chlorobisheptafluoropropylphosphine (8·38 g., 20·7 mmoles) and chlorine (1·47 g., 20·7 mmoles) were sealed in a Carius tube and allowed to warm slowly from −78° to room temperature. The volatile product was *trichlorobisheptafluoropropylphosphorane* (9·54 g., 97%) (Found: Cl, 22·1. $C_6Cl_3F_{14}P$ requires Cl, 22·2%). The vapour pressure (at 50—120°) was given by $\log_{10} p$(mm.) = 7·46 − 2094/*T*. The b. p. was 184° ± 2°, the latent heat of evaporation 9580 cal./mole, and Trouton's constant 20·8. There was slow decomposition at 125° in 16 hr.: chloroheptafluoropropane, identified by its infrared spectrum, dichloroheptafluoropropylphosphine, and chlorobisheptafluoropropylphosphine (0·108 g.) were produced. Hydrolysis of trichlorobisheptafluoropropylphosphorane (0·218 g., 0·458 mmole) with excess of 20% sodium hydroxide solution at room temperature (48 hr.) gave heptafluoropropane (0·0778 g., 0·458 mmole) and, when the alkaline hydrolysate was evaporated to dryness, the infrared spectrum of the residue indicated the presence of disodium heptafluoropropylphosphonate. Aqueous hydrolysis of trichlorobisheptafluoropropylphosphorane gave no heptafluoropropane.

(d) *Aminobisheptafluoropropylphosphine.* Chlorobisheptafluoropropylphosphine (2·23 g., 5·5 mmoles) and sodium-dried ammonia (0·189 g., 11·1 mmoles) were condensed together at −46° and allowed to warm to room temperature. The product on fractionation gave *aminobisheptafluoropropylphosphine* (2·082 g., 98%) (Found: C, 17·9; H, 0·5; N, 4·3; NH_2 as NH_3, 4·0; C_3F_7, 88·4. $C_6H_2F_{14}NP$ requires C, 18·7; H, 0·5; N, 3·6; NH_2, 4·15; C_3F_7, 87·8%). The product was a colourless liquid. The vapour pressure (at 20—120°) was given by $\log_{10} p$(mm.) = 7·743 − 2022/*T*. The b. p. was 143° ± 1°, the latent heat of evaporation 9250 cal./mole, Trouton's constant 22·2, and the m. p. −23°. The compound (0·306 g., 0·794 mmole) was hydrolysed slowly by 15% sodium hydroxide solution and gave heptafluoropropane (0·272 g., 1·59 mmoles). A second sample (0·147 g., 0·383 mmole) was sealed with 2N-hydrochloric acid (5 ml.) for three weeks and gave heptafluoropropane (0·0645 g., 0·379 mmole) and 0·376 mmole of ammonia in the hydrolysate. Hydrolysis by water at room temperature was very slow but at 100° the amine (0·449 g., 1·165 mmoles) gave in 48 hr. 0·263 g. (1·545 mmoles) of heptafluoropropane, indicating partial hydrolysis of the ammonium bisheptafluoropropylphosphinite formed in the first stage. The presence of this salt was confirmed by the infrared spectrum of the solid left on freeze-drying of the aqueous hydrolysate.

(e) *Ethyl bisheptafluoropropylphosphinite.* Chlorobisheptafluoropropylphosphine (3·73 g., 9·23 mmoles) and ethanol (0·432 g., 9·21 mmoles), when shaken at room temperature, gave *ethyl bisheptafluoropropylphosphinite* (3·55 g., 93%) (Found: C, 21·5; H, 1·8; C_3F_7, 81·4; P, 8·0. $C_8H_5F_{14}OP$ requires C, 23·2; H, 1·2; C_3F_7, 81·6; P, 7·5%). The vapour pressure (at 30—120°) was given by $\log_{10} p$(mm.) = 8·17 − 2190/*T*. The b. p. was 140—141°, the latent heat 10,020 cal./mole, Trouton's constant 24·3, and the m. p. −47°. Hydrolysis of the compound by

20% alkali at 20° was incomplete in 12 hr., even with shaking, but was quantitative after several days. When ethyl bisheptafluoropropylphosphinite (0·158 g., 0·383 mmole) was shaken with water for 5 days only 0·004 g. of heptafluoropropane was liberated. When the products were resealed and heated at 150° for 24 hr. a further 0·0105 g. (0·062 mmole) of heptafluoropropane was formed. The compound was apparently immiscible with water and, after heating, two layers were still present. *Ethyl bistrifluoromethylphosphinite* was prepared similarly from chlorobistrifluoromethylphosphine [1] (Found: C, 22·8; H, 2·5; CF_3, 64·7; P, 15·6%; *M*, 214. $C_4H_5F_6OP$ requires C, 22·5; H, 2·3; CF_3, 64·5; P, 14·5%; *M*, 214). The vapour pressure (at −25° to 55°) was given by $\log_{10} p(\text{mm.}) = 7{\cdot}890 - 1739/T$. The b. p. was 74° ± 1°, the latent heat 7960 cal./mole, and Trouton's constant 22·9. The compound was decomposed rapidly and completely by 20% aqueous sodium hydroxide at 20°. A sample (0·136 g., 0·668 mmole), when sealed for 1 week with water at 20°, gave 0·0485 g. (0·695 mmole) of trifluoromethane. When the tube was resealed and heated at 120° for 12 hr. a further 0·0450 g. (0·642 mmole) of trifluoromethane was evolved.

Preparation of Heptafluoropropylphosphonous Acid.—Dichloroheptafluoropropylphosphine (1·9 g., 7·0 mmoles) was added to water (0·252 g., 14·0 mmoles) and gave a clear liquid without evolution of heptafluoropropane. When distilled through a column this gave *heptafluoropropylphosphonous acid* (1·18 g., 72%) (Found: C_3F_7, 71·4; P, 13·4%; equiv., 230. $C_3H_2F_7O_2P$ requires C_3F_7, 72·2; P, 13·3%; equiv., 234). The titration curve was characteristic of a strong monobasic acid with complete neutralisation at pH 7—8. Heptafluoropropylphosphonous acid was decomposed quantitatively to heptafluoropropane by excess of 15% sodium hydroxide solution. There was slow decomposition by water at 100° and heptafluoropropane was again liberated. The acid was slowly but almost quantitatively oxidised by a solution of iodine buffered with sodium hydrogen carbonate. When 20 ml. of solution containing 0·0535 mmole of acid were mixed with 50 ml. of 3% mercuric chloride solution and 50 ml. of 3% glacial acetic acid (5 ml.) there was no precipitate in the cold but, in 12 hr. at 60°, 0·0242 g. (0·0572 mmole) of mercurous chloride was precipitated.

Preparation of Heptafluoropropylphosphonic Acid.—Dichloroheptafluoropropylphosphine (3·43 g.) was added to water (5 ml.) and treated with 50% unstabilised hydrogen peroxide (10 ml.). Freeze-drying gave deliquescent needles of *heptafluoropropylphosphonic acid dihydrate* (3·2 g.) (Found: equiv., 142. $C_3H_6O_5F_7P$ requires equiv., 143). The crystalline *dianilinium salt* was prepared by reaction with excess of aniline in ethanol [Found: C, 41·5; H, 3·5; N, 6·5. $C_3H_7{\cdot}PO(OH)_2{\cdot}2C_6H_5{\cdot}NH_2$ requires C, 41·3; H, 3·7; N, 6·4%]. Similar reaction with one equivalent of aniline gave the *monoaniline salt* which recrystallised from ethanol [Found: C, 31·8; H, 2·9; N, 4·3. $C_3H_7{\cdot}PO(OH)_2{\cdot}C_6H_5{\cdot}NH_2$ requires C, 31·5; H, 2·6; N, 4·1%]. Hydrolysis of the dianiline salt (0·614 g.) with an equivalent quantity of 0·25N-sodium hydroxide gave *disodium heptafluoropropylphosphonate* (0·354 g.) [Found: C, 12·2; H, 0·3%; equiv. (by elution on ion-exchange column and titration), 146. $C_3F_7{\cdot}PO(ONa)_2$ requires C, 12·25; H, 0·6%; equiv., 147]. The sodium salt gave no heptafluoropropane in 20% sodium hydroxide solution at 125° during 48 hr.

Preparation of Bisheptafluoropropylphosphinic Acid.—Distilled water was added dropwise to trichlorobisheptafluoropropylphosphorane (9·54 g.). When slightly more than the stoicheiometric amount had been added the product became solid. Volatile products were pumped off, leaving *bisheptafluoropropylphosphinic acid* (6·42 g.) as a deliquescent white solid [Found: equiv., 406. $(CF_3)_2PO{\cdot}OH$ requires equiv., 402]. The titration curve was typical of that for a strong monobasic acid. When 0·163 g. (0·406 mmole) of the acid was sealed with excess of sodium hydroxide solution (2 days) 0·066 g. (0·30 mmole) of heptafluoropropane was evolved. The infrared spectrum of the solid residue from the hydrolysate after evaporation showed the presence of disodium heptafluoropropylphosphonate. The solid acid sublimed undecomposed in a vacuum at 66—68°.

Silver bisheptafluoropropylphosphinate was prepared by adding silver oxide to the acid and recrystallised from ether [Found: C, 13·6; Ag, 20·7. $(C_3F_7)_2PO{\cdot}OAg$ requires C, 14·1; Ag, 21·2%]. Its hydrolysis was similar to that of the free acid. The *aniline salt* was also prepared [Found: C, 29·7; H, 2·1; N, 3·2%; equiv., 490. $(C_3F_7)_2PO{\cdot}OH{,}C_6H_5{\cdot}NH_2$ requires C, 29·1; H, 1·7; N, 2·8%; equiv., 495].

Reaction of Heptafluoroiodopropane with Arsenic.—In preliminary experiments heptafluoroiodopropane and arsenic were heated in a stainless-steel autoclave (300 ml.) at 200° for 48 hr. The volatile product was a clear yellow liquid, 87% of which distilled at 58—61°/20 mm. There

was no sign of separation into fractions and analysis of the distillate by alkaline hydrolysis gave: C_3F_7, 49·5; As, 10·0; I, 15·4% (Total 74·9%). After hydrolysis, a drop of oil remained which was unattacked by alkali or aqua regia. Its infrared spectrum showed strong absorption at 1450—1000 cm.$^{-1}$, the region of the C–F stretching frequencies. The oil was, therefore, probably fluorocarbon, which could well form azeotopes with the heptafluoropropyl arsenicals. In further experiments the reaction temperature was reduced to minimise fluorocarbon formation, and the volatile products were analysed for C_3F_7, As, and I. At 147°, after 9 hours' heating the yield of arsenicals was 4% and no oil remained on hydrolysis of the volatile reaction product. Heating at 153° gave 10% of fluorocarbon.

The ultraviolet absorption in light petroleum (Pet) and as vapour (V) between 450 and 200 mμ of the halogenoheptafluoropropylphosphines, recorded on a Cary recording spectrophotometer, is tabulated.

Ultraviolet absorption of the halogenoheptafluoropropylphosphines.

		$\lambda_{max.}$	ε	$\lambda_{min.}$	ε
$C_3F_7PI_2$	Pet	270	3700	248	2880
		222	5900	213	5820
$(C_3F_7)_2PI$	Pet	286	1100	253	710
	V	287	1400	250	570
		220	2700	211	2400
$C_3F_7PCl_2$	Pet	223—233	600	—	—
	V	223—230	740		
$(C_3F_7)_2PCl$	Pet	233	270	221	200

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UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE. [*Received, August 27th*, 1958.]

68. *A Quantitative Study of the Arylation of Naphthalene by Means of Diazonium Salts and Zinc.*

By B. A. MARSHALL and WILLIAM A. WATERS.

Free radicals generated by the decomposition, with zinc powder, of acetone suspensions of four aryldiazonium salts have been used to effecthomolytic monosubstitution of naphthalene in both the α- and the β-position. The resulting mixtures of α- and β-arylnaphthalenes have been separated and analysed spectroscopically, comparison being made with synthesised pure reference compounds. The variation in the α : β ratios for the arylations is tabulated and discussed.

NORMAN and WATERS [1] have demonstrated the wide scope, for homolytic arylation of organic solids, inherent in Waters's reaction [2] whereby aryldiazonium salts, in acetone or ethyl acetate suspension, give free aryl radicals on treatment with zinc and similar metals:

$$2Ar{\cdot}N_2^+ + Zn \longrightarrow 2Ar\cdot + 2N_2 + Zn^{2+}$$

This reaction, which was shown to yield both α- and β-phenylnaphthalene from naphthalene, has now been used for the substitution into naphthalene at 20—50° by phenyl, *p*-nitrophenyl, *p*-methoxyphenyl, and *p*-acetamidophenyl free radicals. In each instance the mixed isomeric α- and β-arylnaphthalene have been separated chromatographically from other products and then analysed spectroscopically, authentic reference compounds having been synthesised by unequivocal methods for comparison.

Naphthalene was in every instance used in considerable excess as a concentrated solution in acetone, so as to avoid disubstitution and possible differential loss thereby of either the α- or the β-monosubstituted product. Recoveries and product yields are listed

[1] Norman and Waters, *J.*, 1958, 167.
[2] Waters, *J.*, 1939, 864.

in Table 1. The percentage purity of the mixtures of arylnaphthalenes was estimated by comparing the total weight of any mixture isolated with that calculated from the infrared spectrum of a weighed sample.

TABLE 1. *Quantitative arylation of naphthalene by* p-$R{\cdot}C_6H_4$ *radicals.*

Group R and Source	$C_{10}H_8$ used (mole)	Radical source (mole)	$C_{10}H_8$ recovered (mole)	$R{\cdot}C_6H_4{\cdot}C_{10}H_7$ obtained (mole)	(% purity)
NO_2	0·16	0·08	0·141	0·012	99·6
$Ar{\cdot}N_2{\cdot}BF_4$	0·16	0·08	0·117	0·016	99·3
H	0·16	0·04	0·144	0·004	96·7
$(Ar{\cdot}N_2)_2ZnCl_4$	0·16 *	0·04	0·133	0·007	93·0
NH·COMe	0·16	0·08	0·129	0·003	98·6
$Ar{\cdot}N_2{\cdot}BF_4$	0·20	0·08	0·164	0·009	100·0
OMe	0·16	0·06	0·141	0·007	100·0
$(Ar{\cdot}N_2)_2ZnCl_4$	0·16	0·06	0·125	0·008	80·0

* Benzene used as co-solvent.

A high percentage of the generated $R{\cdot}C_6H_4{\cdot}$ radicals inevitably attack the acetone, forming benzene derivatives $R{\cdot}C_6H_5$, with consequent low yields of arylated naphthalenes. In one instance benzene was used as co-solvent for the phenylation of naphthalene, but the formation of diphenyl then complicated the separation and a trace of bis-4-diphenylyl (quaterphenyl) was also formed.

TABLE 2. *Isomer percentages obtained in the arylation of naphthalene by* p-$R{\cdot}C_6H_4{\cdot}$ *radicals.*

R	α (%)	β (%)	R	α (%)	β (%)
NO_2	83·3, 83·1	16·7, 16·9	NH·COMe	77·0, 76·5	23·0, 23·5
H	80·7, 80·0	19·3, 20·0 *	OMe	74·1, 73·5	25·9, 26·5

* Benzene used as co-solvent.

The isomer percentages given in Table 2 for the phenylation of naphthalene in acetone accord with those determined by Huisgen and Grashey [3] in a series of solvents at about the same temperature, using *N*-nitrosoacetanilide, and with the results of Davies, Hey, and Williams [4] using benzoyl peroxide at 85°. The *para*-substituents alter the α : β ratios slightly, though to an extent far beyond the possible analytical error.

Theoretical calculations show that naphthalene has a higher electron-availability at α- than at β-positions. In accordance with this, heterolytic electrophilic substitution of naphthalene below 100° always gives much more α- than β-isomer. As Table 2 shows, the homolytic substitution into naphthalene by the *p*-nitrophenyl group results in an increased percentage of α-compound, as would be expected for a slightly electrophilic substituting agent. The other two substituents have opposite electrical character and both definitely depress the α : β ratio. This sequence is in the order of Hammett's σ constants for the relative rates of reactions involving aromatic side-chains, but the magnitudes of the relative effects of NO_2, H, NH·COMe, and OMe groups accord better with the σ^+ constants of Brown and Okamoto [5] for reactions in which carbon atoms of aromatic nuclei are directly involved. However, too few figures concerning naphthalene are yet available for discussion of the type of σ factors that should be apposite for the small dipole effects influencing this particular example of homolytic aromatic substitution.

EXPERIMENTAL

Phenylation of Naphthalene in Acetone.—Benzenediazonium zincichloride, prepared by addition of concentrated aqueous zinc chloride (0·2 mole) to aniline (0·3 mole) diazotised in concentrated hydrochloric acid, was collected, washed with alcohol and ether, and stored under dry

[3] Huisgen and Grashey, *Annalen*, 1957, **607**, 46.
[4] Davies, Hey, and Williams, *J.*, 1958, 1878.
[5] Brown and Okamoto, *J. Amer. Chem. Soc.*, 1957, **79**, 1913.

ether at −10°. This solid (16 g.), vigorously stirred in a cold solution of naphthalene (20 g.) in dry acetone (50 ml.), was treated portionwise with zinc powder (6 g.) so that smooth reaction occurred. When no diazonium salt remained (test with H-acid) the solvent was removed on the water-bath and the residue was thoroughly extracted with hot benzene. The filtered extract was evaporated to dryness and the product, in light petroleum (b. p. 40—60°)–benzene (3 : 1), was passed through an alumina column. Most of the naphthalene (18·5 g.; m. p. 80°) was removed from the resulting mixture by crystallisation from methanol, and the remainder, together with the mother-liquors from the crystallisation, was fractionally distilled through a short column, giving the mixed phenylnaphthalenes (0·82 g.) as an oil, b. p. 120—220°/0·5 mm. This was dissolved in " AnalaR " carbon disulphide and its infrared spectrum was measured over the 11—15 μ band, both at the concentration given and after further dilution (1 : 4) with carbon disulphide, in a Perkin-Elmer recording spectrophotometer, Model 21. Infrared spectra were also recorded for solutions of both α- and β-phenylnaphthalene in carbon disulphide at concentrations of 89 mg./25 ml. From these the approximate composition of the mixture was calculated, by using the absorption maxima at 12·5 μ for the α-isomer and 12·25 μ for the β-isomer with correction for the background absorption of the solvent. Thereupon, a series of synthetic mixtures of pure α- and β-phenylnaphthalene was prepared covering, in stages, the range from 80·2 to 81·2% in α-isomer content and thereby a spectrum of a synthetic mixture matching that of the reaction product was found. The deduced composition of the latter was 80·7 ± 0·2% of α-isomer.

Phenylation of Naphthalene in Benzene.—A similar reaction was performed using benzene (50 ml.) plus acetone (5 ml.) as solvent. After removal of naphthalene (17 g.) the mixed phenylnaphthalenes were found to contain 80·0 ± 0·2% of α-isomer. Further elution of the alumina column with benzene gave 4 mg. of a solid, m. p. 312—313°, having log ε 4·61 at $\lambda_{max.}$ 2980 Å; this probably being bis-4-diphenylyl, m. p. 312°, log ε 4·59 at $\lambda_{max.}$ 2980 Å.[6]

p-*Nitrophenylation of Naphthalene in Acetone.*—*p*-Nitrobenzenediazonium fluoroborate (100 g.) was obtained by adding cold saturated aqueous sodium fluoroborate (50 g.) to the product of diazotisation of *p*-nitroaniline (69 g.) in aqueous hydrochloric acid (300 ml. of 1 : 1) with sodium nitrite (35 g. in 80 ml. of water). The yellow solid, after being washed with cold water and then alcohol, was stored under dry ether at −10°. Arylation of naphthalene (20 g.) in dry acetone (50 ml.) was carried out with this diazonium salt (19 g.) and zinc (6 g.) as described above. The benzene-soluble products were chromatographed through alumina (type H) with light petroleum–benzene (9 : 1) which removed naphthalene (18 g.), and then with a 1 : 1 mixture of the same solvents which separated the *p*-nitrophenylnaphthalenes (2·988 g.) from residual tar. This mixture, in carbon disulphide (250 ml.), was analysed spectroscopically, as above, by means of the absorption band of the pure α-isomer at 12·9 μ and of the mixed isomers at 12·3 μ, which is an absorption maximum for the β-compound, the final comparison again being made with synthetic mixtures, giving α-isomer contents of 83·3 ± 0·2% and 83·1 ± 0·2% in a complete duplicate experiment.

p-*Acetamidophenylation of Naphthalene.*—This was conducted with *p*-acetamidobenzenediazonium fluoroborate, as in the previous example. The isomeric α- and β-*p*-acetamidophenylnaphthalene (0·471 g.) were too insoluble in carbon disulphide for accurate measurement of their infrared spectra, whilst solutions in nitromethane or dimethylformamide had too much background absorption in the 11—15 μ wave-band. Use was therefore made of the ultraviolet spectrum of the mixture in ethanol (100 ml.), a record covering the band 3500—2100 Å being taken on a Carey recording spectrophotometer, model 14M-50. Records were also taken of the spectra of the two pure isomers. From the following data (where gram extinction coefficients are given, *i.e.*, ε in ml. g.$^{-1}$ cm.$^{-1}$), the composition of the mixture of isomers was computed by the method of Dewar and Urch,[7] giving replicate values for the α-isomer of 77·0 ± 0·5% and 76·5 ± 0·5%.

Compound	$\lambda_{max.}$ (Å)	ε	Compound	$\lambda_{max.}$ (Å)	ε
α-*p*-Acetamidophenylnaphthalene (1·203 mg. in 100 ml. of alcohol)	2915	57,930	β-*p*-Acetamidophenylnaphthalene (1·531 mg. in 500 ml. of alcohol)	2965	116,300
	2540	56,180		2715	208,200
	2235	240,600		2235	186,200

p-*Methoxyphenylation of Naphthalene.*—This was conducted as for phenylation, using the diazonium zincichloride prepared from *p*-anisidine. Chromatographic separation of

[6] Gillam and Hey, *J.*, 1939, 1170.
[7] Dewar and Urch, *J.*, 1957, 345.

naphthalene (18 g.) and isomeric *p*-methoxyphenylnaphthalenes (1·605 g.) was followed by spectrographic analysis, in the infrared region, in a carbon disulphide solution, with, for comparison, the absorption maximum of the α-isomer at 12·9 μ and of the β-isomer at 13·44 μ, final comparison again being made with synthetic mixtures.

Syntheses of Reference Compounds.—*α-Phenylnaphthalene.* The Grignard reagent from α-bromonaphthalene was condensed with *cyclo*hexanone and the product was dehydrated and then dehydrogenated with palladium–charcoal at 340—360° to α-phenylnaphthalene, b. p. 142—147°/0·5 mm., n_D^{20} 1·6644 (lit.,[8] n_D^{20} 1·6646).

β-Phenylnaphthalene. Phenylacetaldehyde was self-condensed to give β-phenylnaphthalene by refluxing it with hydrobromic acid,[9] and the product, m. p. 101—102° (lit., 101°), was crystallised from acetic acid and then from 1 : 1 ethanol–methanol.

α- and β-p-Nitrophenylnaphthalene. The preparation of the mixed isomers, described above, was repeated several times and a quantity of the mixture was carefully chromatographed through alumina. On elution with light petroleum–benzene (3 : 1) the α-isomer separated first. From alcohol it gave pale yellow needles, m. p. 132—133° (Kühling,[10] by reaction between naphthalene and *p*-nitrobenzene diazohydroxide, obtained orange needles, m. p. 129°) (Found: C, 76·8; H, 4·5; N, 5·7. Calc. for $C_{16}H_{11}O_2N$: C, 77·1; H, 4·7; N, 5·6%). β-*p*-Nitrophenylnaphthalene was thereafter separated with 1 : 1 light petroleum–benzene; it crystallised from alcohol in yellow needles, m. p. 174°. The same compound was obtained on decomposition of neutral diazotised β-naphthylamine solution, together with nitrobenzene, as described by Hey and Lawton.[11] This procedure yielded, in quantity, β-*p*-nitrophenylnaphthalene as a red powder, m. p. 174° (as described), but this, evidently containing some impurity, after sublimation at 140—200°/0·01 mm. gave a yellow solid which, from alcohol, gave yellow needles, m. p. 174° (Found: C, 77·3; H, 4·5; N, 5·6%).

α-p-*Acetamidophenylnaphthalene.* α-*p*-Nitrophenylnaphthalene (0·5 g.) was reduced to α-*p*-aminophenylnaphthalene (0·4 g.) by stannous chloride in alcoholic hydrochloric acid, and then acetylated. The *acetamido-compound* crystallised from light petroleum (b. p. 60—80°)–benzene (1 : 1) in needles, m. p. 198—199° (Found: C, 82·8; H, 5·8; N, 5·6. $C_{18}H_{15}ON$ requires C, 82·7; H, 5·8; N, 5·4%). β-*p*-Acetamidophenylnaphthalene, prepared similarly, crystallised from alcohol in plates, m. p. 206—207° (lit.,[11] m. p. 206°).

α-*p*-Methoxyphenylnaphthalene was prepared by treating *p*-methoxyphenylmagnesium bromide with 1-tetralone and then dehydrating and dehydrogenating the product.[12] It crystallised from 70% ethanol in needles, m. p. 116° (lit., 116·5°) (Found: C, 86·7; H, 6·1. Calc. for $C_{17}H_{14}O$: C, 87·1; H, 6·0%).

β-p-*Methoxyphenylnaphthalene* was separated from the mixture of isomers obtained by the diazo-reaction described above, being eluted from alumina less easily than the α-isomer. The pure β-compound crystallised in plates, m. p. 136—137° (Found: C, 86·6; H, 5·9%). Its infrared absorption spectrum had peaks at 8·0 μ (ether) and at 11·95, 12·05, 12·30, 12·70, and 13·5 μ (1 : 2-, 1 : 4-, and 1 : 2 : 4-substituted benzene).

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THE DYSON PERRINS LABORATORY, OXFORD. [*Received, September 10th*, 1958.]

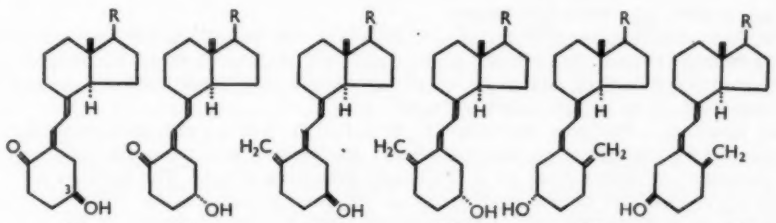
[9] Orchin and Reggel, *J. Amer. Chem. Soc.*, 1947, **69**, 505.
[8] Bailey and Case, *Tetrahedron*, 1958, **3**, 129.
[10] Kühling, *Ber.*, 1896, **29**, 165.
[11] Hey and Lawton, *J.*, 1940, 374.
[12] Howell and Robertson, *J.*, 1936, 587.

69. *Partial Synthesis of Vitamins D_2 and D_3.*

By H. H. Inhoffen, K. Irmscher, H. Hirschfeld, U. Stache, and A. Kreutzer.

Syntheses of *epi*-vitamins D_2 and D_3 have been effected on the lines used before for the natural series. Harrison and Lythgoe's synthesis of vitamin D_2 rested on an unsuspected partial resolution by chromatography and led them to some erroneous identifications.

After preparation of 5 : 6-*trans*-vitamins D_2 and D_3 and their photoisomerisation to the natural (5 : 6-*cis*-)vitamins D_2 and D_3,[1-3] the remaining problem for partial synthesis of the natural vitamins was separation of the 3-hydroxy-epimers. For this we used the mixture[4] of the " dienolone " (I; R = C_9H_{17}) and its *epi*-isomer (II; R = C_9H_{17}), as well as the analogous mixture[5] (I + II; R = C_8H_{17}). Chromatography yielded, without difficulty, the two pairs of pure epimers; as expected each mixture was found to contain its epimers in a 1 : 1 ratio.



(I) (II) (III) (IV) (V) (VI)

The Wittig reaction, with methylenetriphenylphosphorane, converted the four hydroxy-ketones into the four pure triene-alcohols, namely, (III; R = C_9H_{17} and C_8H_{17}) and the *epi*-forms (IV; R = C_9H_{17} and C_8H_{17}).

Of these, the former pair (III) were identical with normal 5 : 6-*trans*-vitamin D_2 and D_3 respectively.[3,6,7] Our photoisomerisation of this pair, by glass-filtered ultraviolet light, to the natural (5 : 6-*cis*-)vitamins D_2 and D_3 (V; R = C_9H_{17} and C_8H_{17} respectively) has already been described.[3] We have now similarly photoisomerised the pure *epi*-5 : 6-*trans*-trienes (IV; R = C_9H_{17} and C_8H_{17}) to the (new) *epi*-vitamins D_2 and D_3 (VI; R = C_9H_{17} and C_8H_{17} respectively). These have not yet crystallised; moreover, their esters do not crystallise well and have unsharp melting points.

Harrison and Lythgoe[8] have also reported a partial synthesis of vitamin D_2. They photoisomerised our " dienolone " epimer mixture (I + II; R = C_9H_{17}), by our method, before introducing the methylene group by the Wittig procedure. Esterification of their mixed product gave the esters of natural (3β-)vitamin D_2 and *epi*(3α)-vitamin D_2 in a 1 : 3-ratio. However, in varying our procedure they chromatographed the dienolone *epimer* mixture (I + II): they discarded a fraction (15%) consisting of *epi*(3α)-rich dienolone

[1] Inhoffen, Kath, Sticherling, and Brückner, *Angew. Chem.*, 1955, **67**, 276; Inhoffen, Quinkert, Hess, and Hirschfeld, *Naturwiss.*, 1957, **44**, 11.
[2] Inhoffen, Kath, Sticherling, and Brückner, *Annalen*, 1957, **603**, 25.
[3] Inhoffen, Quinkert, Hess, and Hirschfeld, *Chem. Ber.*, 1957, **90**, 2544.
[4] Inhoffen, Brückner, and Gründel, *ibid.*, 1954, **87**, 1.
[5] Inhoffen, Irmscher, Hirschfeld, Stache, and Kreutzer, *ibid.*, 1958, **91**, in the press.
[6] Inhoffen, Quinkert, Hess, and Erdmann, *Chem. Ber.*, 1956, **89**, 2273.
[7] Verloop, Koevoet, and Havinga, *Rec. Trav. chim.*, 1955, **74**, 1125.
[8] Harrison and Lythgoe, *Proc. Chem. Soc.*, 1957, 261; *J.*, 1958, 837.

thus producing unwittingly a mixture rich in normal (β-)form and so eventually the unequal proportions of esters which they recorded. In fact the epimeric esters cannot be separated by crystallisation as described if the original 1 : 1 ratio of the mixture (I + II) is maintained. (In the strict sense Harrison and Lythgoe's synthesis is thus not reproducible.) Harrison and Lythgoe's so-called *epi*-vitamin D_2 is, further, a 1 : 1 epimeric mixture. Our earlier sample of *trans*-vitamin D_2 [2] is, as stated, a mixture ($\alpha : \beta = 87 : 13$) and not " practically pure *epi*-vitamin D_2 " as Harrison and Lythgoe believed.

Experimental

Rotations refer to benzene solutions unless otherwise stated. $\lambda_{max.}$ are for ether solutions. Light petroleum had b. p. 40—60°.

Separation of Dienolones.—(*a*) The dienolone epimer mixture [4] (I + II; R = C_9H_{17}) (2·9 g.) was chromatographed in 85 : 15 benzene–ether on alumina (580 g.; Woelm, neutral, grade 2). After rejection of two fractions (together 3·4 l.), fractions 3 and 4 (together 3 l.) yielded compound (I; R = C_9H_{17}), which after crystallisation from ether–light petroleum (yield, 0·71 g., 25%), had m. p. 142·5—144°, $[\alpha]_D$ 218°, $\lambda_{max.}$ 300 mμ (ε 25,200) (Found: C, 81·3; H, 10·4. Calc. for $C_{27}H_{42}O_2$: C, 81·4; H, 10·6%). After removal of intermediate fractions 5—8 (total 2 l.), fractions 9—23 (8 l.) afforded, after recrystallisation, the *epi*-form (0·69 g., 24%), m. p. 132—133·5°, $[\alpha]_D$ +106°, $\lambda_{max.}$ 300 mμ (ε 26,200).

(*b*) Similarly, the mixture (I + II; R = C_8H_{17}) {4 g.; m. p. 143—143·5°, $[\alpha]_D$ +143°, $\lambda_{max.}$ 301 mμ (ε 26,800) (Found: C, 80·9; H, 10·8. Calc. for $C_{26}H_{42}O_2$: C, 80·8; H, 10·95%)}, gave the compound (I; R = C_8H_{17}) (1·45 g.), m. p. 141—141·5°, $[\alpha]_D$ +200°, and the *epi*-form (II; R = C_8H_{17}) (1·53 g.), m. p. 125—126°, $[\alpha]_D$ +88°.

Wittig Reactions.—The pure dienolone (I; R = C_9H_{17}) (0·45 g.) and methylenetriphenylphosphorane (2·1 g.) in ether were boiled for 3 hr.; the product, isolated in the usual way, was chromatographed on alumina (45 g.) in 7 : 3 light petroleum–ether. The fraction with $\lambda_{max.}$ 272—273 mμ crystallised from a similar solvent mixture, giving a triene (III; R = C_9H_{17}) (0·2 g., 45%), m. p. 98·5—101°, $[\alpha]_D$ +216°, identical with 5 : 6-*trans*-vitamin D_2.[6,7]

Similarly, the epimeric dienolone (II; R = C_9H_{17}) (0·45 g.) gave the epi-*triene* (IV; R = C_9H_{17}) (0·19 g., 43%), m. p. 129·5—131·5°, $[\alpha]_D$ +52·5°, $\lambda_{max.}$ 272—273° mμ (ε 24,500) (Found: C, 85·0; H, 10·4. $C_{28}H_{44}O$ requires C, 84·8; H, 11·2%).

Also, in the D_3 series, where R = C_8H_{17}, the dienolone (I) [5] (0·45 g.) gave the triene (III) (0·16 g., 36%), m. p. 88—92°, $[\alpha]_D$ +212° (in ether), identical with 5 : 6-*trans*-vitamin D_3 [3,7]; and the *epi*-compound (II) (0·75 g.) gave the *epi*-triene (IV) (0·22 g.), m. p. 114—116°, $[\alpha]_D$ +47°, $\lambda_{max.}$ 272—273 mμ (ε 25,800).

Photoisomerisations.—Irradiation, effected as before,[3] of the *epi*-triene (IV; R = C_9H_{17}) (0·94 g.) for 9 hr. and chromatography in 7 : 3 light petroleum–ether on alumina (150 g.) gave the (5 : 6-*cis*-)*epi*-vitamin D_2 (VI) as an oil (0·37 g.), $\lambda_{max.}$ 265 mμ (ε 14,800), whose 3 : 5-dinitrobenzoate (0·22 g.) had m. p. 97—100°, $[\alpha]_D$ +4°.

The *epi*-triene (IV; R = C_8H_{17}) (0·4 g.), on irradiation for 8·5 hr. and chromatography (on alumina, 75 g.), gave an oily (5 : 6-*cis*-)*epi*-vitamin D_3 (VI) (0·19 g.), $\lambda_{max.}$ 265 mμ (ε 14,000), whose 3 : 5-*dinitrobenzoate* (0·07 g.) had m. p. 96—100°, $[\alpha]_D$ −1° (Found: C, 70·5; H, 8·2; N, 4·9. $C_{34}H_{46}O_6N_2$ requires C, 70·6; H, 8·0; N, 4·8%).

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70. *Oxidation of Polyhalogeno-compounds. Part II.*[1] *Photolysis and Photochemical Oxidation of Some Chlorofluoroethanes.**

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The vapour-phase photolysis and photochemical oxidation of the compounds $CF_3{\cdot}CCl_3$, $CF_3{\cdot}CHCl_2$, and $CF_3{\cdot}CH_2Cl$ have been studied. Oxidation of the compounds $CF_3{\cdot}CHCl_2$ and $CF_3{\cdot}CH_2Cl$ gives trifluoroacetyl chloride and trifluoroacetic acid. This is a new and convenient route for the preparation of this acid. Yields are greatly increased when chlorine is used as initiator. The compound $CF_3{\cdot}CCl_3$ is oxidised to carbonyl fluoride, but yields trifluoroacetic acid when water is present. Reaction mechanisms are proposed.

In Part I[1] the photochemical vapour-phase oxidation of compounds of the type $CF_3{\cdot}[CF_2]_n{\cdot}CFXY$ (X or Y = H, F, Cl, Br, or I) was described. It was shown that by carrying out the reaction in the presence of water, or by the use of bromine or chlorine as sensitiser, carbon–carbon bond cleavage could often be substantially prevented, so that the corresponding perfluoro-carboxylic acid or -acyl fluoride was obtained. A free-radical mechanism was proposed for these reactions. The present paper is concerned (*a*) with the photolysis and photochemical oxidation of the readily available 1 : 1 : 1-trichlorotrifluoroethane, 1 : 1-dichloro-2 : 2 : 2-trifluoroethane and 1-chloro-2 : 2 : 2-trifluoroethane, (*b*) with the establishment of conditions for their conversion in high yield into trifluoroacetyl chloride or trifluoroacetic acid, and (*c*) with the mechanism of these photolytic and photochemical oxidations.

Light of wavelength >2200 Å was used, with silica reaction vessels. Molecular oxygen was added to effect photochemical oxidation. Despite the high resistance of these chlorofluoroethanes to attack by conventional acidic, basic, or oxidising agents, photochemical oxidation is often rapid and quantitative. The main problem is to control the photochemical oxidation so that carbon–carbon cleavage does not predominate, to give only carbonyl halides and their decomposition products. Such carbon–carbon cleavage can occur by degradation of a perhalogenoalkoxy-radical,[1] or by photolysis of an initial oxidation product such as trifluoroacetic acid or trifluoroacetyl chloride. In general, an initiator, usually chlorine, is advantageous, since it enables the irradiation time to be shortened, and water can be added to convert the readily photolysed trifluoroacetyl chloride into aqueous trifluoroacetic acid; the last technique is particularly necessary for 1 : 1 : 1-trichlorotrifluoroethane which is oxidised photochemically only slowly, and at a rate comparable with that of trifluoroacetyl chloride, its oxidation product.

Typical results are given in Table 1 and the main features are now summarised:

1 : 1 : 1-*Trichlorotrifluoroethane.*—This compound is resistant to concentrated acids and alkalis and to conventional nucleophilic reagents such as ethoxide ion; it gives trifluoroacetic acid in 10% yield only with oleum in presence of mercury salts.[2] The vapour-phase photolysis was slow (54% in 36 days) and yielded the dimer:

$$2CF_3{\cdot}CCl_3 \xrightarrow{h\nu} CF_3{\cdot}CCl_2{\cdot}CCl_2{\cdot}CF_3 + Cl_2$$

Vapour-phase photochemical oxidation was much faster (85% in 2 days) and gave none of the dimer, but a small amount (2%) of trifluoroacetyl chloride, carbon dioxide, and, by attack on the reaction vessel, silicon tetrafluoride. In presence of chlorine or bromine the yield of the acyl chloride was increased, and presence of water or aqueous alkali during

* Preliminary communication, *Proc. Chem. Soc.*, 1957, 146. Presented at Amer. Chem. Soc. Meeting, New York, 1957.

[1] Part I, Francis and Haszeldine, *J.*, 1955, 2151.

[2] Benning and Park, U.S.P. 2,396,076/1946; *Chem. Abs.*, 1946, **40**, 3128.

the photolysis produced a marked increase in yield of trifluoroacetic acid (51%); highest yields (65%) were obtained when both water and chlorine or bromine were present.

TABLE 1. *Photochemical oxidation of some chlorofluoroethanes.*

Mole ratio O_2 : Compound	Initial press. (atm.)	Other reactants	Time of irradiation (hr.)	Oxidation (%)	Product (% yield)	
		Oxidation of $CF_3{\cdot}CCl_3$				
5·3	1·9	—	48	85	$CF_3{\cdot}COCl$	2
4·6	2·6	$Cl_2(Cl_2 : O_2 = 1 : 6)$	48	64	$CF_3{\cdot}COCl$	7
4·4	2·6	$Br_2(Br_2 : O_2 = 1 : 4)$	51	62	$CF_3{\cdot}COCl$	7
2·8	3·3	H_2O	60	68	$CF_3{\cdot}CO_2H$	51
2·4	3·1	$Cl_2(Cl_2 : O_2 = 1·7 : 1), H_2O$	77	80	$CF_3{\cdot}CO_2H$	64
2·5	2·2	$Br_2(Br_2 : O_2 = 1·7 : 1), H_2O$	124	81	$CF_3{\cdot}CO_2H$	65
		Oxidation of $CF_3{\cdot}CHCl_2$				
11·0	1·5	—	5·0	99	$CF_3{\cdot}CO_2H$ $CF_3{\cdot}COCl$	16 60
4·5	1·8	—	6·0	100	$CF_3{\cdot}CO_2H$ $CF_3{\cdot}COCl$	13 60
4·2	2·5	$Cl_2(Cl_2 : O_2 = 1 : 1·9)$	0·08	100	$CF_3{\cdot}CO_2H$ $CF_3{\cdot}COCl$	11 80
4·9	2·8	$Cl_2(Cl_2 : O_2 = 1 : 1·7)$	0·5	100	$CF_3{\cdot}COCl$	90
5·2	2·7	$Cl_2(Cl_2 : O_2 = 1 : 2·1)$	1·2	100	$CF_3{\cdot}CO_2H$ $CF_3{\cdot}COCl$	7 82
5·8	2·4	$Br_2(Br_2 : O_2 = 1 : 1·7)$	113	79	$CF_3{\cdot}CO_2H$	2
2·5	1·7	H_2O	72	100	$CF_3{\cdot}CO_2H$	71
2·5	1·8	$Cl_2(Cl_2 : O_2 = 1 : 1·2), H_2O$	72	100	$CF_3{\cdot}CO_2H$	73
		Oxidation of $CF_3{\cdot}CH_2Cl$				
2·2	1·8	—	31	40	$CF_3{\cdot}CO_2H$	53
2·3	2·2	$Cl_2(Cl_2 : O_2 = 1 : 2·0)$	0·4	49	$CF_3{\cdot}CO_2H$ $CF_3{\cdot}COCl$	16 61
2·5	2·0	$Br_2(Br_2 : O_2 = 1 : 3·8)$	116	18	—	—
2·0	1·8	H_2O	174	76	$CF_3{\cdot}CO_2H$	47
1·9	1·9	$Cl_2(Cl_2 : O_2 = 1 : 1·6), H_2O$	72	100	$CF_3{\cdot}CO_2H$	75

1 : 1-*Dichloro*-2 : 2 : 2-*trifluoroethane*.—The vapour-phase photolysis of this compound was more rapid than for 1 : 1 : 1-trichlorotrifluoroethane:

$$CF_3{\cdot}CHCl_2 \xrightarrow{h\nu} \underset{35\%}{CF_3{\cdot}CHCl{\cdot}CCl_2{\cdot}CF_3} + \underset{6\%}{CF_3{\cdot}CHCl{\cdot}CHCl{\cdot}CF_3} + \underset{3\%}{CF_3{\cdot}CCl_2{\cdot}CCl_2{\cdot}CF_3} + \underset{48\%}{HCl}$$

2 : 2 : 3-Trichloro-1 : 1 : 1 : 4 : 4 : 4-hexafluorobutane was identified by comparison with a sample prepared by the following route:

$$CF_3{\cdot}CCl{:}CCl{\cdot}CF_3 \xrightarrow{Zn\text{–}EtOH} CF_3{\cdot}C{\equiv}C{\cdot}CF_3 \xrightarrow{HCl,\ 300^\circ} CF_3{\cdot}CH{:}CCl{\cdot}CF_2$$

$$CF_3{\cdot}CH{:}CCl{\cdot}CF_2 \xrightarrow{Cl_2,\ h\nu} CF_3{\cdot}CHCl{\cdot}CCl_2{\cdot}CF_3$$

The vapour-phase photochemical oxidation of 1 : 1-dichloro-2 : 2 : 2-trifluoroethane was also much more rapid than that of 1 : 1 : 1-trichlorotrifluoroethane and gave a mixture of trifluoroacetyl chloride (60%) and trifluoroacetic acid (13%). The addition of chlorine greatly increased the rate of oxidation (100% oxidation in 5 min.) and improved the yields of the required products ($CF_3{\cdot}COCl$ 80%; $CF_3{\cdot}CO_2H$ 11%). Unexpectedly, however, the presence of bromine reduced the rate of oxidation, and carbon dioxide and silicon tetrafluoride were then the main products. The ethane was also photochemically oxidised in the presence of water (yield of $CF_3{\cdot}CO_2H$ 71%), and water and chlorine (yield of $CF_3{\cdot}CO_2H$ 73%).

1-*Chloro*-2 : 2 : 2-*trifluoroethane*.—The vapour-phase photolysis of this ethane was

slower than that of 1 : 1-dichloro-2 : 2 : 2-trifluoroethane but faster than that of 1 : 1 : 1-trichlorotrifluoroethane:

$$CF_3{\cdot}CH_2Cl \xrightarrow{h\nu} \underset{31\%}{CF_3{\cdot}CHCl{\cdot}CHCl{\cdot}CF_3} + \underset{31\%}{CF_3{\cdot}CH_3} + \underset{3\%}{CF_3{\cdot}CH_2{\cdot}CH_2{\cdot}CF_3} + \underset{33\%}{HCl}$$

Photochemical oxidation of 1-chloro-2 : 2 : 2-trifluoroethane gave results in general similar to those obtained for 1 : 1-dichloro-2 : 2 : 2-trifluoroethane; presence of chlorine increased the rate of reaction and improved the yields of trifluoroacetyl chloride and trifluoroacetic acid, whereas bromine inhibited the reaction.

Discussion.—The three chlorofluoroethanes discussed above are readily made from tri- or tetra-chloroethylene:

$$CHCl{:}CCl_2 \xrightarrow{HF} CF_3{\cdot}CH_2Cl \xrightarrow{Cl_2} CF_3{\cdot}CHCl_2 \xrightarrow{Cl_2} CF_3{\cdot}CCl_3$$

$$C_2Cl_4 \xrightarrow{Cl_2} C_2Cl_6 \xrightarrow{SbF_3} CF_3{\cdot}CCl_3$$

The present work establishes that their $-CH_2Cl$, $-CHCl_2$, or $-CCl_3$ group can be oxidised to $-COCl$ or $-CO_2H$ in good or excellent yield. This provides a new and convenient route for the synthesis of trifluoroacetic acid. In a laboratory the oxidations can be effected on a half-mole scale by use of the apparatus described earlier.[3]

(a) *Photolysis of the chlorofluoroethanes.* The photolysis of 1 : 1 : 1-trichlorotrifluoroethane to give 2 : 2 : 3 : 3-tetrachlorohexafluoroethane and chlorine is accounted for by the following scheme:

$$CF_3{\cdot}CCl_2{\cdot} \xrightarrow{h\nu} CF_3{\cdot}CCl_2{\cdot} + Cl{\cdot}$$
$$2CF_3{\cdot}CCl_2{\cdot} \longrightarrow CF_3{\cdot}CCl_2{\cdot}CCl_2{\cdot}CF_3$$
$$Cl{\cdot} + Cl{\cdot} \longrightarrow Cl_2$$

The products resulting from the photolysis of 1 : 1-dichloro-2 : 2 : 2-trifluoroethane suggest the following scheme:

$$CF_3{\cdot}CHCl_2 \xrightarrow{h\nu} CF_3{\cdot}CHCl{\cdot} + Cl{\cdot} \quad \ldots\ldots\ldots (1)$$
$$CF_3{\cdot}CHCl_2 + Cl{\cdot} \longrightarrow CF_3{\cdot}CCl_2{\cdot} + HCl \quad \ldots\ldots\ldots (2)$$
$$2CF_3{\cdot}CHCl{\cdot} \longrightarrow CF_3{\cdot}CHCl{\cdot}CHCl{\cdot}CF_3 \quad \ldots\ldots\ldots (3)$$
$$CF_3{\cdot}CHCl{\cdot} + CF_3{\cdot}CCl_2{\cdot} \longrightarrow CF_3{\cdot}CHCl{\cdot}CCl_2{\cdot}CF_3 \quad (4)$$
$$2CF_3{\cdot}CCl_2{\cdot} \longrightarrow CF_3{\cdot}CCl_2{\cdot}CCl_2{\cdot}CF_3 \quad \ldots\ldots\ldots (5)$$

Step 2 accounts both for the observed formation of hydrogen chloride and for the faster photolysis of the dichloro-compound than of 1 : 1 : 1-trichlorotrifluoroethane.

The photolysis products of 1-chloro-2 : 2 : 2-trifluoroethane are similarly accounted for by the sequence:

$$CF_3{\cdot}CH_2Cl \xrightarrow{h\nu} CF_3{\cdot}CH_2{\cdot} + Cl{\cdot} \quad \ldots\ldots\ldots (6)$$
$$CF_3{\cdot}CH_2Cl + Cl{\cdot} \longrightarrow CF_3{\cdot}CHCl{\cdot} + HCl \quad \ldots\ldots\ldots (7)$$
$$CF_3{\cdot}CH_2{\cdot} + CF_3{\cdot}CH_2Cl \longrightarrow CF_3{\cdot}CH_3 + CF_3{\cdot}CHCl{\cdot} \quad \ldots\ldots\ldots (8)$$
$$2CF_3{\cdot}CHCl{\cdot} \longrightarrow CF_3{\cdot}CHCl{\cdot}CHCl{\cdot}CF_3 \quad \ldots\ldots\ldots (9)$$
$$2CF_3{\cdot}CH_2{\cdot} \longrightarrow CF_3{\cdot}CH_2{\cdot}CH_2{\cdot}CF_3 \quad \ldots\ldots\ldots (10)$$
$$CF_3{\cdot}CH_2{\cdot} + CF_3{\cdot}CHCl{\cdot} \longrightarrow CF_3{\cdot}CH_2{\cdot}CHCl{\cdot}CF_3 \quad \ldots\ldots\ldots (11)$$

Steps 7 and 8 account for the formation of hydrogen chloride (33%) and 1 : 1 : 1-trifluoroethane (31%) respectively, and lead to a relatively high concentration of $CF_3{\cdot}CHCl{\cdot}$ radicals which dimerise to give the observed 2 : 3-dichloro-1 : 1 : 1 : 4 : 4 : 4-hexafluorobutane (31%). The $CF_3{\cdot}CH_2{\cdot}$ radical is rapidly consumed by step 8 rather than by steps 10 and 11 since the

[3] Barr and Haszeldine, *J.*, 1955, 1881.

starting material is present in excess. Although a small quantity of 1 : 1 : 1 : 4 : 4 : 4-hexafluorobutane was isolated, none of the expected 2-chloro-1 : 1 : 1 : 4 : 4 : 4-hexafluorobutane (reaction 11) was found. The overall reaction is thus predominantly:

$$3CF_3{\cdot}CH_2Cl \longrightarrow CF_3{\cdot}CH_3 + CF_3{\cdot}CHCl{\cdot}CHCl{\cdot}CF_3 + HCl$$

(b) *Photochemical oxidation of* 1 : 1 : 1-*trichlorotrifluoroethane.* The photochemical oxidation of 1 : 1 : 1-trichlorotrifluoroethane is explained by the following scheme:

$$CF_3{\cdot}CCl_3 \xrightarrow{h\nu} CF_3{\cdot}CCl_2{\cdot} + Cl{\cdot} \quad (12)$$

$$CF_3{\cdot}CCl_2{\cdot} + O_2 \longrightarrow CF_3{\cdot}CCl_2{\cdot}O_2{\cdot} \quad (13)$$

$$CF_3{\cdot}CCl_2{\cdot}O_2{\cdot} + Cl{\cdot} \longrightarrow CF_3{\cdot}CCl_2{\cdot}O{\cdot}OCl \quad (14)$$

$$CF_3{\cdot}CCl_2{\cdot}O_2{\cdot} + CF_3{\cdot}CCl_3 \longrightarrow CF_3{\cdot}CCl_2{\cdot}O{\cdot}OCl + CF_3{\cdot}CCl_2{\cdot} \quad (14a)$$

$$\downarrow O_2$$

$$CF_3{\cdot}CCl_2{\cdot}O_2{\cdot} \longrightarrow \text{etc.}$$

$$CF_3{\cdot}CCl_2{\cdot}O{\cdot}OCl \longrightarrow CF_3{\cdot}CCl_2{\cdot}O{\cdot} + {\cdot}OCl \quad (15)$$

$$CF_3{\cdot}CCl_2{\cdot}O{\cdot} \longrightarrow CF_3{\cdot}COCl + Cl{\cdot} \quad (16)$$

$$CF_3{\cdot}CCl_2{\cdot}O{\cdot} \longrightarrow CF_3{\cdot} + COCl_2 \quad (17)$$

$$COCl_2 \xrightarrow{O_2} CO_2 + Cl_2 \quad (18)$$

$$CF_3{\cdot} \xrightarrow{O_2} CF_3{\cdot}O_2{\cdot} \longrightarrow CF_3{\cdot}O{\cdot} \xrightarrow{SiO_2} CO_2 + SiF_4 \quad (19)$$

which is similar to that suggested earlier for photochemical oxidation of perhalogeno-radicals.[1] The following facts support this.

First, the occurrence of step 12 is required by the results obtained when 1 : 1 : 1-trichlorotrifluoroethane was photolysed alone.

Secondly, the much greater rate of photochemical oxidation than of photolysis in absence of oxygen is to be attributed to the very rapid combination of $CF_3{\cdot}CCl_2{\cdot}$ radicals with oxygen (step 13), thus preventing reversal of the primary step:

$$CF_3{\cdot}CCl_2{\cdot} + Cl_2 \longrightarrow CF_3{\cdot}CCl_3 + Cl{\cdot}$$

Evidence for the rapidity of the combination of the $CF_3{\cdot}CCl_2{\cdot}$ radical with oxygen also arises from studies on 1 : 1-dichloro-2 : 2 : 2-trifluoroethane in presence of chlorine; it is noteworthy that the $CF_3{\cdot}CCl_2{\cdot}$ radical produced by hydrogen abstraction:

$$CF_3{\cdot}CHCl_2 + Cl{\cdot} \longrightarrow CF_3{\cdot}CCl_2{\cdot} + HCl$$

rapidly combines with chlorine to give 1 : 1 : 1-trichlorotrifluoroethane quantitatively when oxygen is absent, whereas when both chlorine and oxygen are present only the oxidation products of the $CF_3{\cdot}CCl_2{\cdot}$ radical result, and not even a trace of 1 : 1 : 1-trichlorotrifluoroethane can be found.

Thirdly, the formation of the $CF_3{\cdot}CCl_2{\cdot}O{\cdot}$ radical by steps 13—15 can be followed by elimination of a chlorine atom to give trifluoroacetyl chloride (step 16), or by carbon–carbon fission to give carbonyl chloride and a trifluoromethyl radical (step 17) which then breaks down as outlined earlier.[1]

Fourthly, one can account for the increased yield of trifluoroacetyl chloride in the presence of added chlorine or bromine, and the formation of trifluoroacetic acid when water (yield of $CF_3{\cdot}CO_2H$ 51%), or water and halogen (yield of $CF_3{\cdot}CO_2H$ 65%), are present. A radical such as $CF_3{\cdot}CCl_2{\cdot}O{\cdot}$, which contains chlorine on the α-carbon atom, breaks down mainly by loss of a chlorine atom rather than by carbon–carbon bond fission; separate experiments show that the failure to isolate more than very small quantities (2%) of trifluoroacetyl chloride when 1 : 1 : 1-trichlorotrifluoroethane is oxidised in absence

of water is caused by the faster photochemical oxidation of trifluoroacetyl chloride under these conditions. Aqueous trifluoroacetic acid is photochemically oxidised only very slowly, and when water is present to remove trifluoroacetyl chloride as formed, the yield of trifluoroacetic acid is increased.

The presence of an excess of halogen stabilises the acyl chloride by reversal of its primary photolysis step:

$$CF_3{\cdot}COCl \xrightarrow{h\nu} CF_3{\cdot}CO{\cdot} + Cl{\cdot}$$

Direct reaction of an intermediate species such as $CF_3{\cdot}CCl_2{\cdot}O{\cdot}Cl$ with water could also serve as a source of trifluoroacetic acid, so that the yield of the acid is not necessarily a measure of the extent to which step **16** predominates over step **17**.

(c) *Photochemical oxidation of* **1 : 1-***dichloro-***2 : 2 : 2-***trifluoroethane.* This provides further information about the relative occurrence of oxidation to trifluoroacetyl chloride and carbon–carbon fission, and the effect of added water. The great ease of oxidation is caused by the chlorine produced by the primary photolysis reaction (1), reacting as in reaction (2); addition of chlorine as initiator markedly increases the oxidation rate. The major product in absence of added water is trifluoroacetyl chloride (60%); the trifluoroacetic acid (13%) also formed arises by hydrolysis of trifluoroacetyl chloride by water also produced during the oxidation. The much greater yield of trifluoroacetyl chloride thus obtained compared with that in the oxidation of 1 : 1 : 1-trichlorotrifluoroethane (2%), even though both involve $CF_3{\cdot}CCl_2{\cdot}$ radicals, is attributed to the much shorter irradiation time required which greatly reduces the photochemical decomposition of trifluoroacetyl chloride.

The $CF_3{\cdot}CCl_2{\cdot}$ radical produced by reaction (2) gives rise to trifluoroacetyl chloride (reactions 13—16). The $CF_3{\cdot}CHCl{\cdot}$ radical of step (1) would similarly form the $CF_3{\cdot}CHCl{\cdot}O{\cdot}$ radical, and this could either give trifluoroacetyl chloride by the loss of its hydrogen atom in several ways:

$$CF_3{\cdot}CHCl{\cdot}O{\cdot} \longrightarrow CF_3{\cdot}COCl + H{\cdot}$$
$$CF_3{\cdot}CHCl{\cdot}O{\cdot} + Cl{\cdot} \longrightarrow CF_3{\cdot}COCl + HCl$$
$$CF_3{\cdot}CHCl{\cdot}O{\cdot} + O_2 \longrightarrow CF_3{\cdot}COCl + HO_2{\cdot}$$

or break down by carbon–carbon bond fission:

$$CF_3{\cdot}CHCl{\cdot}O{\cdot} \longrightarrow CF_3{\cdot} + {\cdot}CHClO{\cdot}$$
$$\downarrow O_2 \qquad \downarrow O_2$$
$$CO_2 (+ SiF_4) \qquad CO_2 + H_2O + Cl_2$$

In the absence of added chlorine, $CF_3{\cdot}CCl_2{\cdot}O{\cdot}$ and $CF_3{\cdot}CHCl{\cdot}O{\cdot}$ radicals are produced in approximately equal amounts and since the yield of trifluoroacetyl chloride is well above 50% a substantial part of it must arise from the $CF_3{\cdot}CHCl{\cdot}O{\cdot}$ radicals in one or more of the ways indicated above.

The $CF_3{\cdot}CHCl{\cdot}O$ radical could also break down by loss of a chlorine atom to give trifluoroacetaldehyde. Control experiments with the aldehyde showed that it is readily photolysed in the absence of oxygen to give trifluoromethyl radicals and that it reacts rapidly with chlorine on exposure to ultraviolet light to give chlorotrifluoromethane (54%). The $CF_3{\cdot}CHCl{\cdot}O{\cdot}$ radical when formed by photochemical oxidation of 1-chloro-2 : 2 : 2-trifluoroethane (see below) gives trifluoroacetyl chloride in 77% yield. Since trifluoroacetyl chloride is produced in only very low yield by photochemical chlorination of trifluoroacetaldehyde, it follows that not nore than *ca.* 23% of the $CF_3{\cdot}CHCl{\cdot}O{\cdot}$ radicals can have formed trifluoroacetaldehyde. Thus, if trifluoroacetaldehyde is formed at all in the photochemical oxidation of 1 : 1-dichloro-2 : 2 : 2-trifluoroethane, its maximum yield can only be about 12%.

When chlorine is present so that the molar ratio $CF_3{\cdot}CHCl_2 : Cl_2$ is about 1 : 1, the

photochemical oxidation is complete within a few minutes and trifluoroacetyl chloride is produced in 90% yield. The speed of the reaction and the formation of hydrogen chloride show that initiation must be virtually exclusively by hydrogen abstraction to give $CF_3 \cdot CCl_2 \cdot$ radicals. The $CF_3 \cdot CCl_2 \cdot O$ radicals must also break down by loss of a chlorine atom and only to a small extent by carbon–carbon bond fission. This behaviour is in marked contrast to that of perfluoroalkoxy-radicals which undergo carbon–carbon bond fission exclusively, *e.g.*, in the photochemical oxidation of 1-iodoheptafluoropropane: [1]

$$R_F \cdot CF_2 \cdot O \cdot \longrightarrow R_F \cdot O \cdot + COF_2$$

This may be attributed to the relative energies of the C–F and C–Cl bonds, since the alternative mode of breakdown

$$R_F \cdot CF_2 \cdot O \cdot \longrightarrow R_F \cdot COF + F \cdot$$

would require the breaking of the strong C–F bond.

The photochemical oxidation of 1 : 1 : 1-trichlorotrifluoroethane in presence of water gives a lower yield of trifluoroacetic acid than expected if $CF_3 \cdot CCl_2 \cdot O \cdot$ radicals are intermediates; some of these radicals or other intermediate species must thus react with water by carbon–carbon bond fission. Similarly, the yield of trifluoroacetic acid from 1 : 1-dichloro-2 : 2 : 2-trifluoroethane when both chlorine and water were added (73%) was markedly lower than that of trifluoroacetyl chloride when only chlorine was added (90%).

(d) *Photochemical oxidation of* 1-*chloro*-2 : 2 : 2-*trifluoroethane.* The $CF_3 \cdot CH_2 \cdot$ and $CF_3 \cdot CHCl \cdot$ radicals produced by steps (6) and (7) are similarly considered to give rise to $CF_3 \cdot CH_2 \cdot O \cdot$ and $CF_3 \cdot CHCl \cdot O \cdot$ radicals. The fate of the $CF_3 \cdot CHCl \cdot O \cdot$ radical has been discussed. The $CF_3 \cdot CH_2 \cdot O \cdot$ radical might be expected to behave like a primary hydrocarbon alkoxy-radical, $R \cdot CH_2 \cdot O \cdot$, which [4] reacts by hydrogen-abstraction or by carbon–carbon bond fission to give formaldehyde, *i.e.*,

$$CF_3 \cdot CH_2 \cdot O \cdot + CF_3 \cdot CH_2Cl \longrightarrow CF_3 \cdot CH_2 \cdot OH + CF_3 \cdot CHCl \cdot$$

or

$$CF_3 \cdot CH_2 \cdot O \cdot \longrightarrow CF_3 \cdot + CH_2O$$

$$\downarrow O_2 \qquad \downarrow O_2$$

$$CO_2 (+ SiF_4) \qquad CO_2 + H_2O$$

Control experiments with 2 : 2 : 2-trifluoroethanol show that it is stable to ultraviolet light in absence of oxygen, and that photolysis in presence of chlorine rapidly converts it into 2 : 2 : 2-trifluoroethyl trifluoroacetate (60%), chlorotrifluoromethane (13%), and fluoroform (9%). The ester arises by the intermediate formation of trifluoroacetyl chloride:

$$CF_3 \cdot COCl + CF_3 \cdot CH_2 \cdot OH \longrightarrow CF_3 \cdot CO_2 \cdot CH_2 \cdot CF_3 + HCl$$

Neither trifluoroethanol nor its trifluoroacetate could be detected amongst the photochemical oxidation products of 1-chloro-2 : 2 : 2-trifluoroethane.

The $CF_3 \cdot CH_2 \cdot O \cdot$ radical could also break down by loss of a hydrogen atom:

$$CF_3 \cdot CH_2 \cdot O \cdot \longrightarrow CF_3 \cdot CHO + H \cdot$$

Some distinction can be made between the various possible reaction steps outlined above. Oxidation with oxygen alone gives trifluoroacetic acid (53%) which presumably arises from the hydrolysis of trifluoroacetyl chloride by water also produced during the photolysis. The $CF_3 \cdot CHCl \cdot$ and $CF_3 \cdot CH_2 \cdot$ radicals and hence also the $CF_3 \cdot CHCl \cdot O \cdot$ and $CF_3 \cdot CH_2 \cdot O \cdot$ radicals are produced in approximately equal amounts under these conditions, and some $CF_3 \cdot CH_2 \cdot O \cdot$ radicals must thus give rise to trifluoroacetyl chloride or trifluoroacetic acid. The primary process with chlorine present is almost exclusively hydrogen abstraction, so that only $CF_3 \cdot CHCl \cdot O \cdot$ radicals need be considered; the high yield (CF_3COCl +

[4] See, for example, Levy, *J. Amer. Chem. Soc.*, 1953, **75**, 1801; Levy and Adrian, *ibid.*, 1955, **77**, 2015; Tipper, *Quart. Rev.*, 1957, **4**, 334—337.

$CF_3 \cdot CO_2H$ 77%) shows that this radical is efficiently converted into trifluoroacetyl chloride. The lower yield (53%) in the absence of chlorine shows that most of the $CF_3 \cdot CH_2 \cdot O\cdot$ radicals break down by carbon–carbon fission or *via* trifluoroacetaldehyde.

The failure of bromine to act as a sensitiser in the oxidation of 1-chloro- and 1 : 1-dichloro-2 : 2 : 2-trifluoroethane must be attributed to the inability of a bromine atom to abstract a hydrogen atom, since the photolysis of 1 : 1-dichloro-2 : 2 : 2-trifluoroethane in the presence of bromine gave 1-bromo-1-chloro-2 : 2 : 2-trifluoroethane (68%) as the only bromine-containing product:

$$CF_3 \cdot CHCl_2 \xrightarrow{h\nu} CF_3 \cdot CHCl\cdot \xrightarrow{Br_2} CF_3 \cdot CHClBr$$

and in particular 1-bromo-1 : 1-dichlorotrifluoroethane was not detected. The failure to obtain significant amounts of trifluoroacetyl chloride, trifluoroacetyl bromide, or trifluoroacetic acid from 1 : 1-dichloro-2 : 2 : 2-trifluoroethane in the experiments in which bromine was added is caused by the inhibiting effect of bromine; the irradiation time required to produce a significant degree of oxidation of the starting material was more than sufficient to ensure the complete oxidation of any of these possible products. The reason for the inhibiting effect is not known.

Experimental

The general techniques were described in Part I.[1] The reactants were either commercial samples or were prepared by standard methods; all were distilled before use and were analytically and spectroscopically pure and free from peroxide. Yields are based on material consumed. Only typical experiments are described. Products were identified by their b. p., molecular weight, and infrared spectra; mixtures were analysed by a combination of infrared spectroscopy and chemical analysis.

Photolysis of 1 : 1 : 1-*Trichlorotrifluoroethane.*—1 : 1 : 1-Trichlorotrifluoroethane (0·506 g., 2·98 mmole), sealed in a 320 ml. silica tube and exposed to ultraviolet light for 36 days, gave both liquid and solid products. The volatile products were shaken with mercury in a sealed tube to remove the chlorine produced, then fractionally distilled *in vacuo*, to give only unchanged 1 : 1 : 1-trichlorotrifluoroethane (0·261 g., 1·38 mmole, 46%) (Found: *M*, 187. Calc. for $C_2Cl_3F_3$: *M*, 187·5). The solid was purified by sublimation at atmospheric pressure, to give 2 : 2 : 3 : 3-tetrachlorohexafluorobutane (0·151 g., 0·496 mmole, 76%), spectroscopically identical with a known sample.

2 : 2 : 3 : 3-*Tetrachlorohexafluorobutane.*—2 : 3-Dichlorohexafluorobut-2-ene (1·033 g., 4·45 mmole) and chlorine (0·670 g., 9·44 mmole), sealed in a 50 ml. Pyrex tube, failed to react in the dark during 24 hr. Irradiation with ultraviolet light for 24 hr., followed by removal of the excess of chlorine, gave 2 : 2 : 3 : 3-tetrachlorohexafluorobutane (1·10 g., 3·62 mmole, 82%) (Found: C, 15·7. Calc. for $C_4Cl_4F_6$: C, 15·8%), m. p. 84°, purified by sublimation. Henne *et al.*[5] record m. p. 83—84°.

Photochemical Oxidation of 1 : 1 : 1-*Trichlorotrifluoroethane.*—(i) *With oxygen alone.* 1 : 1 : 1-Trichlorotrifluoroethane (0·538 g., 2·87 mmole) and oxygen (0·486 g., 15·2 mmole) were exposed in a sealed 260 ml. silica tube (initial pressure *ca.* 1·9 atm.) to ultraviolet light for 48 hr. The volatile products were shaken with mercury in a sealed tube to remove chlorine, transferred to a vacuum-system, and fractionally distilled, to give unchanged 1 : 1 : 1-trichlorotrifluoroethane (0·080 g., 0·426 mmole, 15%), trifluoroacetyl chloride (0·005 g., 0·038 mmole, 2%), and a mixture (0·350 g., 5·83 mmole) of carbon dioxide and silicon tetrafluoride.

(ii) *In the presence of chlorine.* In a typical experiment, 1 : 1 : 1-trichlorotrifluoroethane (0·641 g., 3·41 mmole), chlorine (0·346 g., 4·87 mmole), and oxygen (0·512 g., 16·0 mmole) were irradiated in a sealed 260 ml. silica tube (initial pressure *ca.* 2·6 atm.) for 42 hr. The volatile products were treated as in (i), to give 1 : 1 : 1-trichlorotrifluoroethane (0·320 g., 1·71 mmole, 50%), trifluoroacetyl chloride (0·022 g., 0·168 mmole, 10%), and a mixture (0·148 g., 2·46 mmole) of carbon dioxide and silicon tetrafluoride.

(iii) *In the presence of bromine.* 1 : 1 : 1-Trichlorotrifluoroethane (0·716 g., 3·82 mmole), bromine (0·700 g., 4·38 mmole), and oxygen (0·537 g., 16·8 mmole), sealed in a 260 ml. silica tube (initial pressure *ca.* 2·6 atm.), were exposed to ultraviolet light for 51 hr. The volatile products were treated as in (i), to give 1 : 1 : 1-trichlorotrifluoroethane (0·272 g., 1·45 mmole,

[5] Henne, Hinkamp, and Zimmerscheid, *J. Amer. Chem. Soc.*, 1945, **67**, 1906.

38%), trifluoroacetyl chloride (0·022 g., 0·168 mmole, 7%), and a mixture (0·300 g., 5·00 mmole) of carbon dioxide and silicon tetrafluoride.

(iv) *In the presence of water.* 1 : 1 : 1-Trichlorotrifluoroethane (1·091 g., 5·82 mmole), water (2·5 ml.), and oxygen (0·513 g., 16·0 mmole), sealed in a 150 ml. silica tube (initial pressure *ca.* 3·3 atm.) and exposed to ultraviolet light for 60 hr., gave unchanged 1 : 1 : 1-trichlorotrifluoroethane (0·345 g., 1·84 mmole, 32%) and carbon dioxide (0·020 g., 0·454 mmole). The aqueous solution was treated with an excess of silver carbonate, filtered, and freeze-dried. The residue was extracted with ether, and the ethereal extract was evaporated *in vacuo*, to give analytically and spectroscopically pure silver trifluoroacetate (0·450 g., 2·04 mmole, 51%). In presence of 5N-sodium hydroxide and under similar conditions, the yield of silver trifluoroacetate was 51%.

(v) *In the presence of water and chlorine.* 1 : 1 : 1-Trichlorotrifluoroethane (1·246 g., 6·65 mmole), water (3·0 ml.), chlorine (0·668 g., 9·41 mmole), and oxygen (0·504 g., 15·8 mmole) in a 260 ml. silica tube (initial pressure *ca.* 3·1 atm.), irradiated for 76 hr., gave chlorine (removed by reaction with mercury), unchanged 1 : 1 : 1-trichlorotrifluoroethane (0·250 g., 1·33 mmole, 20%), and carbon dioxide (0·040 g., 0·91 mmole). The aqueous solution was treated as in (iv), to give spectroscopically pure silver trifluoroacetate (0·753 g., 3·38 mmole, 64%).

(vi) *In the presence of water and bromine.* 1 : 1 : 1-Trichlorotrifluoroethane (1·171 g., 6·24 mmole), bromine (1·450 g., 9·07 mmole), water (3·0 ml.), and oxygen (0·497 g., 15·5 mmole), sealed in a 320 ml. silica tube, were exposed to ultraviolet light for 124 hr. The products, treated as in (iv), were shown to be 1 : 1 : 1-trichlorotrifluoroethane (0·228 g., 1·22 mmole, 19% recovery), carbon dioxide (0·085 g., 1·93 mmole), and trifluoroacetic acid identified as silver trifluoroacetate (0·733 g., 3·32 mmole, 65%).

Photolysis of 1 : 1-*Dichloro*-2 : 2 : 2-*trifluoroethane.*—(i) *Alone.* 1 : 1-Dichloro-2 : 2 : 2-trifluoroethane (1·402 g., 9·16 mmole) was exposed in a sealed 320 ml. silica tube to ultraviolet light for 28 days. Hydrogen chloride (0·160 g., 4·39 mmole, 48%) (Found: *M*, 36·7. Calc. for HCl: *M*, 36·5) was the only volatile product. The higher-boiling products were distilled at atmospheric pressure through a semi-micro Vigreux column to give: (*a*) a mixture shown spectroscopically and by molecular-weight determination to consist of 2 : 3-dichloro-1 : 1 : 1 : 4 : 4 : 4-hexafluorobutane (0·12 g., 0·51 mmole) and 2 : 2 : 3-trichloro-1 : 1 : 1 : 4 : 4 : 4-hexafluorobutane (0·25 g., 0·94 mmole); (*b*) 2 : 2 : 3-trichloro-1 : 1 : 1 : 4 : 4 : 4-hexafluorobutane (0·50 g., 1·88 mmole), b. p. 104° (Found: C, 18·1; H, 0·8. Calc. for $C_4HCl_3F_6$: C, 17·8; H, 0·4%), spectroscopically identical with a known sample; and (*c*) a mixture shown spectroscopically to consist of 2 : 2 : 3-trichloro-1 : 1 : 1 : 4 : 4 : 4-hexafluorobutane (0·1 g., 0·4 mmole) and 2 : 2 : 3 : 3-tetrachlorohexafluorobutane (0·08 g., 0·26 mmole). The products of photolysis are thus; HCl 48%, $CF_3{\cdot}CHCl{\cdot}CHCl{\cdot}CF_3$ 6%, $CF_3{\cdot}CHCl{\cdot}CCl_2{\cdot}CF_3$ 35%, and $CF_3{\cdot}CCl_2{\cdot}CCl_2{\cdot}CF_3$ 3%.

(ii) *In the presence of bromine.* 1 : 1-Dichloro-2 : 2 : 2-trifluoroethane (0·541 g., 3·54 mmole) and bromine (0·473 g., 2·95 mmole, irradiated in a 150 ml. silica tube for 12 days, gave, after removal of bromine by shaking with mercury, (*a*) 1 : 1-dichloro-2 : 2 : 2-trifluoroethane (0·105 g., 0·696 mmole, 19%), (*b*) hydrogen chloride (0·058 g., 1·56 mmole, 69%), and (*c*) a mixture of 1 : 1 : 1-trifluorobromochloroethane (*ca.* 0·30 g.), 2 : 3-dichloro-1 : 1 : 1 : 4 : 4 : 4-hexafluorobutane (*ca.* 0·08 g.), and 2 : 2 : 3-trichloro-1 : 1 : 1 : 4 : 4 : 4-hexafluorobutane (*ca.* 0·06 g.). The photolysis products are thus: HCl 69%, $CF_3{\cdot}CHClBr$ 68%, $CF_3{\cdot}CHCl{\cdot}CHCl{\cdot}CF_3$ 15%, and $CF_3{\cdot}CHCl{\cdot}CCl_2{\cdot}CF_3$ 9%.

Synthesis of 2 : 2 : 3-*Trichloro*-1 : 1 : 1 : 4 : 4 : 4-*hexafluorobutane.*[6]—Hexafluorobut-2-yne (1·843 g., 11·9 mmole), prepared in 54% yield by dechlorination of 2 : 3-dichlorohexafluorobut-2-ene, and hydrogen chloride (0·495 g., 13·5 mmole) did not react in a 200 ml. Pyrex tube at 200° in 24 hr. Reaction at 300° (24 hr.) gave (*a*) hexafluorobut-2-yne (0·050 g., 0·31 mmole, 30%), (*b*) hydrogen chloride (0·116 g., 3·18 mmole, 24%), (*c*) a mixture (0·477 g.) of 2 : 3-dichloro-1 : 1 : 1 : 4 : 4 : 4-hexafluorobutane and unidentified olefins, and (*d*) 2-chloro-1 : 1 : 1 : 4 : 4 : 4-hexafluorobut-2-ene (1·395 g., 7·04 mmole, 62%) (Found: C, 24·3; H, 0·7%; *M*, 198. Calc. for C_4HClF_6: C, 24·2; H, 0·5%; *M*, 198·5). No reaction took place at temperatures up to 100° in presence of anhydrous ferric or aluminium chloride (cf. Haszeldine [6]). The butene (1·914 g., 9·65 mmole) and chlorine (0·770 g., 10·8 mmole), sealed in a 50 ml. Pyrex tube and exposed to ultraviolet light for 24 hr., gave 2 : 2 : 3-trichloro-1 : 1 : 1 : 4 : 4 : 4-hexafluorobutane (2·47 g., 9·16 mmole, 95%), b. p. 104° (Found: C, 17·9; H, 0·6. Calc. for $C_4HCl_3F_6$: C, 17·8; H, 0·4%).

[6] Henne and Finnegan, *J. Amer. Chem. Soc.*, 1949, **71**, 298; Haszeldine, *J.*, 1952, 2504

Photochemical Oxidation of 1 : 1-*Dichloro*-2 : 2 : 2-*trifluoroethane and* 1-*Chloro*-2 : 2 : 2-*trifluoroethane.*—The experimental procedure was similar to that described for 1 : 1 : 1-trichlorotrifluoroethane and details for typical experiments are summarised in Table 2.

Photolysis of 1-*Chloro*-2 : 2 : 2-*trifluoroethane.*—1-Chloro-2 : 2 : 2-trifluoroethane (14·8 g., 0·124 mmole) was exposed in a sealed 360 ml. silica tube to ultraviolet light for 52 days. A small amount of non-condensable gas was pumped off, and a small amount of free chlorine was removed by mercury. Distillation *in vacuo* gave (*a*) 2 : 2-dichloro-1 : 1 : 1 : 4 : 4 : 4-hexafluorobutane (1·26 g., 5·37 mmole) (Found: *M*, 235. Calc. for $C_4H_2Cl_2F_6$: *M*, 235), (*b*) a mixture of 2 : 3-dichloro-1 : 1 : 1 : 4 : 4 : 4-hexafluorobutane (0·12 g., 0·5 mmole) and 1 : 1 : 1 : 4 : 4 : 4-hexafluorobutane (0·08 g., 0·5 mmole), (*c*) 1-chloro-2 : 2 : 2-trifluoroethane (12·47 g., 0·105 mole, 85%), (*d*) 1 : 1 : 1-trifluoroethane (0·450 g., 5·36 mmole) (Found: *M*, 85. Calc. for $C_2H_3F_3$: *M*, 84) identified spectroscopically, and (*e*) a mixture of 1 : 1 : 1-trifluoroethane (0·039 g., 0·47 mmole) and hydrogen chloride (0·232 g., 6·35 mmole). The products were thus $CF_3{\cdot}CHCl{\cdot}CHCl{\cdot}CF_3$ 31%, $CF_3{\cdot}CH_3$ 31%, $CF_3{\cdot}CH_2{\cdot}CH_2{\cdot}CF_3$ 3%, and HCl 33%.

Photochemical Oxidation of Trifluoroacetyl Chloride.—In a typical experiment, trifluoroacetyl chloride (0·170 g., 1·28 mmole) and oxygen (0·312 g., 9·75 mmole) were exposed in a sealed 260-ml. silica tube (initial pressure *ca.* 1·1 atm.) to ultraviolet light for 2·0 hr. The volatile products (after removal of chlorine with mercury) were fractionally distilled *in vacuo*, to give unchanged trifluoroacetyl chloride (0·138 g., 1·03 mmole, 81%) and a mixture (0·032 g., 0·53 mmole) of carbon dioxide and silicon tetrafluoride.

TABLE 2.

Compound (mmole)	O_2 (mmole)	Other reactants (mmole)	Vol. of tube (ml.)	Initial press. (atm.)	Irradiation time (hr.)	Oxidation (%)	Products * (mmole)	
			Oxidation of $CF_3{\cdot}CHCl_2$					
1·26	13·9	None	260	1·5	5	99	$CF_3{\cdot}CO_2H$	0·193
							$CF_3{\cdot}COCl$	0·730
3·31	15·0	,,	260	1·8	6·0	100	$CF_3{\cdot}CO_2H$	0·421
							$CF_3{\cdot}COCl$	2·00
3·32	13·8	Cl_2 7·12	260	2·5	0·08	100	$CF_3{\cdot}CO_2H$	0·352
							$CF_3{\cdot}COCl$	2·64
3·35	16·4	Cl_2 9·49	260	2·8	0·5	100	$CF_3{\cdot}COCl$	3·00
3·17	16·5	Cl_2 7·72	260	2·7	1·2	100	$CF_3{\cdot}CO_2H$	0·219
							$CF_3{\cdot}COCl$	2·59
2·67	15·6	Br_2 9·41	300	2·4	113	79	$CF_3{\cdot}CO_2H$	0·044
6·74	16·8	H_2O 3·0 ml.	360	1·7	72	100	$CF_3{\cdot}CO_2H$	4·73
6·54	16·6	Cl_2 1·34, H_2O 3·0 ml.	360	1·8	72	100	$CF_3{\cdot}CO_2H$	4·78
			Oxidation of $CF_3{\cdot}CH_2Cl$					
6·77	15·1	None	320	1·8	31	40	$CF_3{\cdot}CO_2H$	1·44
6·88	16·0	Cl_2 8·23	360	2·2	0·4	49	$CF_3{\cdot}CO_2H$	0·53
							$CF_3{\cdot}COCl$	2·05
6·99	17·4	Br_2 3·81	360	2·0	116	18	$CF_3{\cdot}CO_2H$	0
							$CF_3{\cdot}COCl$	0
8·35	17·0	H_2O 5·0 ml.	360	1·8	174	76	$CF_3{\cdot}CO_2H$	2·95
8·76	16·4	Cl_2 10·1, H_2O 3·0 ml.	360	1·9	72	100	$CF_3{\cdot}CO_2H$	6·56

* CO_2, SiF_4, and HCl produced in every experiment.

Photolysis of Trifluoroacetaldehyde.—(i) *Alone.* Trifluoroacetaldehyde (0·254 g., 2·59 mmole) was irradiated in a sealed 200 ml. silica tube with ultraviolet light for 4 hr. The non-condensable gas was pumped off, and the volatile products were distilled *in vacuo*, to give hexafluoroethane (0·097 g., 0·71 mmole, 55%), fluoroform (0·035 g., 0·50 mmole, 19%), and traces of silicon tetrafluoride and carbonyl fluoride. A solid (*ca.* 0·05 g.) remained in the reaction tube.

(ii) *In the presence of chlorine.* Trifluoroacetaldehyde (0·250 g., 2·55 mmole) and chlorine (0·122 g., 1·71 mmole) in a 260 ml. silica tube, exposed to ultraviolet light for 4 hrs., gave (*a*) a mixture of chlorotrifluoromethane (0·143 g., 1·37 mmole), fluoroform (0·051 g., 0·73 mmole), and hydrogen chloride (0·040 g., 1·1 mmole), and (*b*) a fraction (0·050 g.) containing trifluoroacetyl chloride and an unidentified compound containing a carbonyl group.

Photolysis of 2 : 2 : 2-*Trifluoroethanol.*—(i) ***Alone.*** **2 : 2 : 2-Trifluoroethanol** (0·860 g.,

8·60 mmole) was recovered unchanged after exposure to ultraviolet light for 7 days in a 150 ml. silica tube.

(ii) *In the presence of chlorine.* 2 : 2 : 2-Trifluoroethanol (1·100 g., 1·0 mmole) and chlorine (0·829 g., 11·6 mmole) in a 320 ml. silica tube, irradiated for 6 hr., gave 2 : 2 : 2-trifluoroethyl trifluoroacetate (0·650 g., 3·31 mmole, 66%), hydrogen chloride (0·546 g., 15·0 mmole), fluoroform (0·070 g., 1·0 mmole), and chlorotrifluoromethane (0·146 g., 1·40 mmole). A residual high-boiling liquid (*ca.* 0·2 g.) was not investigated.

2 : 2 : 2-*Trifluoroethyl Trifluoroacetate.*—Trifluoroacetic acid (5·7 g., 5·0 mmole), 2 : 2 : 2-trifluoroethanol (5·0 g., 5·0 mmole), and concentrated sulphuric acid (0·2 ml.) were heated under reflux for 3 hr. Distillation gave 2 : 2 : 2-trifluoroethyl trifluoroacetate (7·2 g., 3·69 mmole, 74%), b. p. 56° (Found: C, 24·4; H, 1·1. Calc. for $C_4H_2O_2F_6$: C, 24·5; H, 0·5%). Husted and Ahlbrecht [7] report b. p. 55—56°/741 mm.

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UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE. [*Received, July 28th,* 1958.]

[7] Husted and Ahlbrecht, *J. Amer. Chem. Soc.*, 1952, **74**, 5422.

71. *Thiohydantoins. Part V.* A New Synthesis of 5 : 5-Disubstituted 4-Thiohydantoins.*

By H. C. CARRINGTON, C. H. VASEY, and W. S. WARING.

5 : 5-Disubstituted 4-thiohydantions are formed by the reaction of ketones with ammonium monothiocarbamate and sodium cyanide.

KETONES react with sodium cyanide and ammonium carbonate in the well-known Bucherer reaction to give 5 : 5-disubstituted hydantoins,[1] and replacement of the ammonium carbonate by carbon disulphide and an ammonium salt leads to the formation of the corresponding 2 : 4-dithiohydantoins.[2] The behaviour of carbon oxysulphide or ammonium monothiocarbamate in this reaction is therefore of interest, as in this case it is possible that either the 2- or the 4-monothiohydantoin might be formed. The 2-thiohydantoins are readily available by other methods,[3] but very few members of the 4-thiohydantoin series have been described, and the methods for their preparation are far from satisfactory. 5 : 5-Pentamethylene-4-thiohydantoin,[3] 5 : 5-diphenyl-4-thiohydantoin,[4] and 5-methyl-5-phenyl-4-thiohydantoin [5] have been prepared by methylation of the 2 : 4-dithiohydantoins and hydrolysis of the 2-methylthio-derivatives, but the methylations lead to mixtures of products, the separation of which is tedious, and the yields of the 4-thiohydantoins are low and variable. 5 : 5-Dimethyl-4-thiohydantoin has also been prepared by Hazard *et al.*[6] by a similar method.

Ketones on treatment with ammonium monothiocarbamate and sodium cyanide gave the corresponding 4-thiohydantoins, often in quite good yield.

Aliphatic, *cyclo*alkyl, and alkyl–aralkyl ketones have been used. The 5 : 5-pentamethylene-4-thiohydantoin obtained from *cyclo*hexanone by this method had a melting point slightly higher than that previously described. Further evidence of structure has been obtained in the case of 5-*iso*butyl-5-methyl-4-thiohydantoin by its conversion by phosphorus pentasulphide in boiling tetralin into the known 2 : 4-dithiohydantoin,[2] and by its non-identity with the 2-thio-compound, which has been prepared from the 2 : 4-dithiohydantoin by the action of 2-aminoethanol followed by acid hydrolysis. The ready

* Part IV, *J.*, 1953, 3105.

[1] Bucherer and Steiner, *J. prakt. Chem.*, 1934, **140**, 291; Bucherer and Lieb, *ibid.*, 1934, **141**, 5.
[2] Carrington, *J.*, 1947, 681.
[3] *Idem*, *J.*, 1947, 684.
[4] Carrington and Waring, *J.*, 1950, 354.
[5] Carrington, Vasey, and Waring, *J.*, 1953, 3105.
[6] Hazard, Cheymol, Chabrier, and Smarzewska, *Bull. Soc. chim. France*, 1949, 228.

desulphurisation of the 4-thio-compound by a similar process to give the known 5-*iso*butyl-5-methylhydantoin [7] is additional evidence of the position of the sulphur atom, since it has already been shown [3] that the intermediate 2-hydroxyethylimino-compounds are readily hydrolysed when this substituent is in the 4-position but are very resistant to hydrolysis when it is in position 2. The 4-thiohydantoins are all yellow crystalline solids, in contrast to the 2-thio-compounds which are colourless.

Experimental.—*5 : 5-Disubstituted 4-thiohydantoins.* The ketone (0·1 mole), sodium cyanide (0·2 mole), and ammonium monothiocarbamate (0·2 mole; prepared from carbon oxysulphide and ethanolic ammonia) were stirred in aqueous ethanol (150 c.c.; equal parts by volume) at 50—55° under reflux for 4 hr. The cooled mixture was acidified with hydrochloric acid, and the pale yellow solid was collected and crystallized from ethanol or aqueous ethanol. In some cases it was convenient to purify the product through its colourless sodium salt which was often sparingly soluble and readily crystallized from hot water or methanol.

The 4-thiohydantoins which have been prepared by this method are shown in the Table.

*Some transformations of 5-iso*butyl-5-*methyl*-4-*thiohydantoin.* 5-*iso*Butyl-5-methyl-4-thiohydantoin (0·5 g.) and phosphorus pentasulphide (1·0 g.) were suspended in tetralin (10 c.c.) and boiled under reflux for 45 min. The mixture was filtered hot, light petroleum (b. p. 40—60°; 50 c.c.) was added to the cooled solution and the supernatant liquid was decanted from the gum.

5 : 5-Disubstituted 4-thiohydantoins.

5 : 5-Substituents	M. p.	Yield (%)	Formula	Required (%) C	H	N	Found (%) C	H	N
R, R = Me, Et	232—233°	46	$C_6H_{10}ON_2S$	45·6	6·3	17·7	45·6	6·2	18·0
R, R = Me, Bu^i	198—199	51	$C_8H_{14}ON_2S$	51·6	7·5	15·05	51·5	7·2	14·8
R, R = Me, Me·$[CH_2]_5$	155—156	62	$C_{10}H_{18}ON_2S$	56·1	8·4	13·1	56·2	8·3	13·5
R, R = Me, $PhCH_2$	216—217	67	$C_{11}H_{12}ON_2S$	60·0	5·45	12·7	60·0	5·8	12·7
RR = ·$[CH_2]_4$·	205°—206	14	$C_7H_{10}ON_2S$	49·4	5·9	16·5	49·1	5·7	16·4
RR = ·$[CH_2]_5$·	242—243	49	$C_8H_{12}ON_2S$	(ref. 3)					
RR = ·$[CH_2]_4$·CHMe·	252	22	$C_9H_{14}ON_2S$	54·5	7·1	14·1	54·2	7·2	14·3
RR = ·$[CH_2]_3$·CHMe·CH_2·	279	47	$C_9H_{14}ON_2S$	54·5	7·1	14·1	54·5	6·8	14·1
RR = ·$[CH_2]_2$·CHMe·$[CH_2]_2$·	262	17	$C_9H_{14}ON_2S$	54·5	7·1	14·1	54·4	7·0	14·7
RR = ·$[CH_2]_2$·CH[$CHMe_2$]·CH_2·	262	14	$C_{11}H_{18}ON_2S$	58·4	8·0	12·4	58·5	8·2	11·9
RR = ·CH_2·CHMe·CH_2·CHMe·CH_2·	sublimes at 330	69	$C_{10}H_{16}ON_2S$	56·6	7·55	13·2	56·9	7·6	13·2
RR = ·CH_2·CHMe·CH_2·CMe_2·CH_2·	224—225	57	$C_{11}H_{18}ON_2S$	58·4	8·0	12·4	58·3	8·0	12·2
RR = ·$[CH_2]_2$·$[CHMe]_2$·CH_2·	274—275	—	$C_{10}H_{16}ON_2S$	—	—	13·2	—	—	13·7
RR = ·$[CH_2]_6$·	177—178	51	$C_8H_{14}ON_2S$	54·5	7·1	14·15	54·7	7·2	14·1
RR = ·CHMe·$[CH_2]_5$·	248—249	45	$C_{10}H_{16}ON_2S$	—	—	13·2	—	—	13·3

Further dilution with light petroleum (b. p. 40—60°) precipitated a sticky solid which after trituration with light petroleum (b. p. 100—120°) was readily crystallized from benzene, yielding very pale yellow prisms, m. p. 89—90° undepressed on admixture with an authentic specimen of 5-*iso*butyl-5-methyl-2 : 4-dithiohydantoin.[2]

5-*iso*Butyl-5-methyl-4-thiohydantoin (0·5 g.), 2-aminoethanol (0·5 c.c.), and water (0·5 c.c.) were heated under reflux for 30 min. Hydrogen sulphide was evolved. Hydrochloric acid (20%; 5 c.c.) was added and refluxing was continued for 45 min. The solution was cooled, and the crystals were filtered off and washed with water. The product had m. p. 142—143° undepressed on admixture with an authentic specimen of 5-*iso*butyl-5-methylhydantoin.[7]

5-*iso*Butyl-5-methyl-2 : 4-dithiohydantoin (1 g.), 2-aminoethanol (1 c.c.), and water (5 c.c) were heated under reflux for 30 min. Hydrochloric acid (20%; 25 c.c.) was added, and refluxing was continued for a further 30 min. The solution was cooled, the crystals were filtered off, washed with water, and recrystallized from aqueous methanol, giving 5-iso*butyl-5-methyl-2-thiohydantoin* as crystals, m. p. 152° (Found: C, 51·8; H, 7·6; N, 14·7. $C_8H_{14}ON_2S$ requires C, 51·6; H, 7·5; N, 15·0%). A mixture with the isomeric 4-thiohydantoin (m. p. 198—199°) had m. p. 130—134°.

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ALDERLEY PARK, MACCLESFIELD, CHESHIRE. [*Received, August 1st*, 1958.]

[7] Henze, Thompson, and Speer, *J. Org. Chem.*, 1943, **8**, 17.

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72. *The Kinetics of the Hydrolysis of the Chlorinated Methanes.*

By Ian Fells and E. A. Moelwyn-Hughes.

The kinetics of the hydrolysis of chloroform and carbon tetrachloride have been investigated over a range of temperature in acidic and alkaline aqueous solution. The results, combined with earlier work on methyl chloride and methylene dichloride, give an account of the differing stability towards hydrolysis of the chlorinated methanes.

For chloroform the changes resolve themselves into a very slow first-order reaction with the solvent and a rapid second-order reaction between chloroform and the hydroxyl ion, probably involving the carbon dichloride radical as an intermediate and giving both carbon monoxide and formate ion as products.

Carbon tetrachloride reacts with water more rapidly than methylene dichloride or chloroform. The reaction appears to be of the second order with respect to carbon tetrachloride. The rate of hydrolysis is unaffected by hydrogen ion, hydroxyl ion, or chloride ion.

The effect of temperature on the rates of the acid hydrolysis of the first three members of the series and of the alkaline hydrolysis of chloroform cannot be represented by an equation having only two constants. The variation of the apparent energy of activation with respect to temperature is discussed in terms of the number of solvating water molecules. The data for the remaining reactions can be summarised in equations containing two constants only.

The positions of relevant equilibria have been computed thermodynamically by using spectroscopic data supplemented by static measurements.

A general mechanism of hydrolysis for all the methyl halides and methylene dichloride is discussed in terms of the solvation numbers of the reactants.

It is suggested that the unusual kinetic behaviour of carbon tetrachloride in water may be due to the absence of a carbon–hydrogen bond and thus of a vibration frequency in the solute molecule lying near to one of the three vibration frequencies in the solvent molecule.

This work completes an investigation of the acid and alkaline hydrolysis of the chlorinated methanes. Data on methyl chloride are given by Moelwyn-Hughes,[1] and for methylene dichloride by Fells and Moelwyn-Hughes.[2] The present account concerns the behaviour of chloroform and carbon tetrachloride in water under acid and basic conditions.

Kinetics of the Hydrolysis of Chloroform.

(a) *Hydrolysis of Chloroform in Water.*—The hydrolysis of chloroform in water proceeds extremely slowly even at the b. p. of the solvent. The reaction has been investigated over the temperature range 370—423° K. (In this range the reaction is slow and the solubility low but both are measurable. At higher temperatures the solubility is too low to allow the use of the techniques adopted here.)

Experimental. The sealed-ampoule technique previously described was used to follow the reaction over the temperature range indicated.

Reagents. Chloroform (Harrington Bros. Ltd.) was treated in the same way as methylene dichloride.[2] On distillation the fraction of b. p. 61·15—61·25° (corr.) was collected (lit.,[3] b. p. 61·20°). Vapour-phase chromatography showed that less than 0·01% of other chlorinated methanes were present.

[1] Moelwyn-Hughes, *Proc. Roy. Soc.*, 1949, *A*, **196**, 540; 1953, *A*, **220**, 386.
[2] Fells and Moelwyn-Hughes, *J.*, 1958, 268, 1326.
[3] Timmermans, "Physico-Chemical Constants," Elsevier, Amsterdam, 1950.

Conductivity water from an Amberlite resin column was used for making up all solutions for kinetic runs.

Analysis. The products of the hydrolysis of chloroform in water are carbon monoxide, formic acid, and hydrochloric acid:

$$CHCl_3 + H_2O \longrightarrow CO + 3HCl;\ CHCl_3 + 2H_2O \longrightarrow H{\cdot}CO_2H + 3HCl$$

In general, considerably more carbon monoxide is formed than formic acid. Each sample was analysed for chloride ion and for strong and weak acids. Chloride ion and total hydrogen ion were estimated by the techniques described previously.[2] The indicator used in the determination of total hydrogen ion was phenolphthalein. In addition to obtaining the hydrochloric and formic acid concentrations from the difference between the chloride ion and total hydrogen ion, values were also obtained by conductometric analysis, which confirmed the values obtained by the difference method.

Kinetic analysis and results. The acid hydrolysis of chloroform follows a first-order law; the constants are calculated from the slopes of the plots of the logarithm of the concentration of chloroform against time, using the equation $k_1 = (1/t) \log a/(a - x)$, where a is the initial concentration of chloroform and $a - x$ its concentration after time t. The extent to which the

TABLE 1. *Acid hydrolysis of chloroform at* 373·16° K.

$10^5 k_1 = 7{\cdot}285 \pm 0{\cdot}146$ sec.$^{-1}$.

Time (min.)	$[Cl^-]$ (mmoles/l.)	$[H^+]$ (mmoles/l.)	x mmoles/l. Obs. from Cl^-	Calc. as $a[1 - \exp(-k_1 t)]$
0	0	0	0	0
22,893	2·70	2·90	0·90	0·90
32,688	4·01	4·34	1·34	1·25
44,173	4·70	5·39	1·57	1·64
55,993	5·92	6·44	1·97	2·05
63,043	6·26	6·66	2·09	2·27
70,215	7·68	8·03	2·56	2·46
80,591	7·82	8·40	2·61	2·80
∞	28·32	—	9·43	9·43

hydrolysis gives carbon monoxide or formic acid as product does not affect this kinetic analysis. The results of a specimen run, for which the quarter life was 69,000 min., are given in Table 1. The values of k_1 found at different temperatures do not conform with the integrated two-constant Arrhenius equation but can be represented by the equation:

$$\log_{10} k_1 = 149{\cdot}6905 - 46{\cdot}28 \log_{10} T - 14{,}108/T \quad . \quad . \quad . \quad . \quad . \quad (1)$$

according to which the apparent energy of activation (E_A) decreases with increase in temperature. In this respect chloroform quantitatively resembles methylene dichloride and methyl chloride, but the value of $-\partial E_A/\partial T$ (92 ± 30 cal./deg.) is greater. A comparison of the observed values of k_1 and those reproduced by equation (1) is given in Table 2. The observed values of k_1 are correct to ±2%. The fraction of chloroform molecules reacting to give formic acid is 18%.

TABLE 2.

T (K)	373·16°	404·05°	413·01°	422·94°
$10^5 k_1$ (sec.$^{-1}$), calc.	7·099	139·0	288·2	608·3
$10^5 k_1$ (sec.$^{-1}$), obs.	7·119	138·8	287·8	609·8

Discussion.—It has been quantitatively established that the chemical changes in the hydrolysis of chloroform by water are as given above. Both reactions can proceed by a common rate-determining mechanism which is of first order with respect to the solute, the reactive intermediate formed breaking down rapidly in part to carbon monoxide and in part to formic acid by some such mechanism as the following:

$$HCCl_3 + H{\cdot}OH \xrightarrow{k_1} HCCl_2{\cdot}OH + HCl \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (I)$$

$$HCCl_2{\cdot}OH \longrightarrow H{\cdot}COCl + HCl \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (II)$$

$$H{\cdot}COCl \longrightarrow HCl + CO \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (III)$$

$$H{\cdot}COCl + H_2O \longrightarrow HCl + H{\cdot}CO_2H \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (IV)$$

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The rate-determining step (I) is slower than that of the corresponding step in the hydrolysis of methylene dichloride. The first-order rate constant is one-ninth of that for methylene dichloride at 373° K. The subsequent steps involving the breakdown of the unstable intermediate $HCCl_2{\cdot}OH$ into formyl chloride, and the breakdown and hydrolysis of formyl chloride to give carbon monoxide and formic acid, are probably very rapid. Formyl chloride has not been isolated, but a mixture of carbon monoxide and hydrochloric acid in the presence of a catalyst can be made to behave as though formyl chloride were present (Gatterman–Koch synthesis, 1897). Formyl chloride at 100° would certainly be hydrolysed very rapidly.

Since chloroform reacts with water to give two products other than hydrochloric acid, the changes in the standard free energies for the two reactions in aqueous solution have been calculated in the hope of discovering which reaction is thermodynamically more probable. The thermodynamic treatment is described in detail in our previous paper.[2] The standard free energies have been obtained from the National Bureau of Standards publications, and Henry's constants from International Critical Tables.

For the reaction $CHCl_3 + 2H_2O \longrightarrow H{\cdot}CO_2H + 3HCl$ in aqueous solution at 25° with the products and reactants in their standard states, $\Delta G°$(aq.) = −51,280 cal. For the reaction $CHCl_3 + H_2O \longrightarrow CO + 3HCl$, $\Delta G°$(aq.) = −47,751 cal.

These calculations make it clear that, as far as free-energy considerations go, both reactions are equally probable within the limits of accuracy of the data. On the basis of the suggested mechanism, therefore, it appears that formyl chloride is more likely to break down to carbon monoxide than to hydrolyse to formic acid although the free-energy change is the same. This view is strengthened by the observation that formic acid does not break down to carbon monoxide and water in dilute aqueous solution even at high temperatures.[4]

(b) *Reaction between Chloroform and Aqueous Potassium Hydroxide.*—The kinetics of this reaction have been examined. The concurrent reactions:

$$CHCl_3 + 4OH^- \longrightarrow H{\cdot}CO{\cdot}O^- + 3Cl^- + 2H_2O$$
$$CHCl_3 + 3OH^- \longrightarrow CO + 3Cl^- + 2H_2O$$

have been investigated over the temperature range 288—334° K. It is found that reaction between chloroform and the hydroxide ion takes place so rapidly compared with the solvolysis that the reaction with the solvent can be ignored.

Experimental. The reactions were carried out in the presence of a small volume of vapour (less than 0·5%) in a Pyrex reaction vessel similar in design to the nickel vessel used for the alkaline hydrolysis of methylene dichloride. Samples were removed through a mercury-sealed, grease-free tap. The apparatus was immersed in a water thermostat accurate to ±0·01° over a period of several days.

Analysis. As the alkaline hydrolysis of chloroform proceeds at a measurable rate at room temperature, the reaction cannot be stopped effectively by chilling the sample. Samples removed from the reaction vessel were, therefore, immediately run into excess of nitric acid. Chloride ion, total hydrogen ion, and strong and weak acids were estimated as before.

Kinetic analysis and results. The reaction between chloroform and hydroxide ion is of the second kinetic order, but is complicated by an unusual mechanism (to be discussed later) and the fact that there are two products of hydrolysis other than hydrochloric acid, namely, carbon monoxide and potassium formate. The fraction (g) of chloroform reacting to give formate is found, from the analytical results, to fall from 0·24 at 288° K to 0·10 at 307° K and then to rise to 0·18 at 334° K. A bimolecular constant involving g has been calculated. If a is the initial concentration of chloroform, b that of hydroxide, and $a - x$ that of chloroform after time t, then

$$k_2 = \frac{2{\cdot}303}{t[a(3 + g) - b]} \log_{10} \frac{b(a - x)}{a[b - (3 + g)x]}$$

[4] Barnham and Clark, *J. Amer. Chem. Soc.*, 1951, **73**, 4638.

Hine [5] has used a similar expression for a bimolecular constant in his work on the alkaline hydrolysis of haloforms in mixed solvents.

The results of a specimen run are given in Table 3. The calculated values of chloroform concentrations are obtained by substituting b, g, t, and the adopted value of k_2 into this rate-constant equation. The bimolecular rate constants governing the reaction of chloroform with

TABLE 3. *Alkaline hydrolysis of chloroform at* 307·96° K. (Concentrations in mmoles/l.): $10^4k_2 = 3{\cdot}082 \pm 0{\cdot}093$ l. mole^{-1} sec.$^{-1}$.

Time (min.)	[KOH]	[Cl$^-$]	[$CHCl_3$], obs.	[$CHCl_3$], calc.	Time (min.)	[KOH]	[Cl$^-$]	[$CHCl_3$], obs.	[$CHCl_3$], calc.
0	68·86	0	18·00	18·00	560	46·96	22·08	10·64	10·73
30	66·71	2·09	17·31	17·31	660	44·46	24·59	9·81	9·91
50	66·22	2·73	17·09	17·00	1019	37·15	31·16	7·61	7·59
140	61·70	7·64	15·45	15·59	2622	24·32	42·78	3·74	3·38
270	55·90	13·08	13·64	13·69	∞	—	54·00	0	0
410	50·67	17·91	12·03	11·99					

the hydroxyl ion cannot be fitted to the integrated form of the Arrhenius equation and are best represented by the three-constant equation:

$$\log_{10}k_2 = 212{\cdot}80249 - 67{\cdot}18\log_{10}T - 15{,}132/T \quad . \quad . \quad . \quad . \quad . \quad (2)$$

TABLE 4.

T (K)	288·19°	298·06°	307·96°	317·90°	334·41°
10^5k_2 (l. mole^{-1} sec.$^{-1}$), obs.	1·140	6·527	30·82	111·2	925·5
10^5k_2 (l. mole^{-1} sec.$^{-1}$), calc.	1·133	6·465	30·85	125·5	936·6

The observed values of k_2 are compared with those reproduced by equation (2) in Table 4. The change of the apparent activation energy with temperature is:

$$\partial E_A/\partial T = -133{\cdot}5 \pm 35 \text{ cal./deg.}$$

The observed values of k_2 are correct to $\pm 2\%$. A forced fit to an equation of the Arrhenius type is:

$$\log_{10}k_2 = 16{\cdot}0141 - 27{,}582/2{\cdot}303RT$$

The effect of added salts on k_2 is shown in Table 5. In the absence of hydroxide, chloroform showed no chlorine–iodide exchange with iodide ion after 10,000 min. at 307·96° K.

TABLE 5.

Added salt	Concn. (mmoles/l.)	10^4k_2 at 307·96°K (l. mole^{-1} sec.$^{-1}$)
None	—	$3{\cdot}08 \pm 0{\cdot}09$
KNO_3	100	$3{\cdot}02 \pm 0{\cdot}06$
KCl	90	$2{\cdot}66 \pm 0{\cdot}05$
KI	85	$1{\cdot}99 \pm 0{\cdot}10$ gradually increasing with time

Discussion.—The hydrolysis of chloroform in neutral or acidic aqueous solution resembles, in many ways, that of methyl chloride and methylene dichloride, but is about nine times slower than that of the latter and 1800 times slower than that of the former at 373° K. Kinetically the reaction is of the first order with respect to the solute. The energy of activation and the rate of decrease of the energy of activation with respect to the temperature are both higher for chloroform than for methyl chloride and methylene dichloride. The mechanism and general characteristics of the reaction appear to be the same as for the first two members of the series.

It was expected by analogy with the solvent reaction of methyl chloride and methylene dichloride that the second-order constant for the reaction between chloroform and hydroxide ion would be lower than that for methylene dichloride. The experimentally

[5] Hine, *J. Amer. Chem. Soc.*, 1950, **72**, 2438.

determined ratios for $CH_3Cl : CH_2Cl_2 : CHCl_3$ at 373° K are 830 : 5·5 : 10,000. The three unusual features in the alkaline hydrolysis of chloroform are its unexpectedly high rate, the effect of added salts, and the decrease of the activation energy with increase in temperature.

The kinetics of the alkaline hydrolysis of the trihalogenated methanes have been investigated in detail by Hine *et al.*[5-8] whose conclusions are qualitatively confirmed by the present work: their rate constants are about 25% lower than the values obtained in this work. The discrepancy in experimental results may well be due to differences in techniques. The type of reaction vessels used by Hine *et al.* allowed a relatively large vapour phase (3—4% of the liquid phase) and the reactions were carried out in excess of chloroform, so that the reaction stopped as soon as the hydroxide ion had been consumed. They discussed several reaction mechanisms. On the basis of the experimental evidence then available the most likely mechanism appeared to be a rapidly established equilibrium giving CCl_3^- ions, followed by a rate-determining unimolecular breakdown of CCl_3^-:

$$(1)\quad CHCl_3 + OH^- \overset{\text{Fast}}{\rightleftharpoons} CCl_3^- + H_2O$$

$$(2)\quad CCl_3^- \overset{\text{Slow}}{\rightleftharpoons} CCl_2 + Cl^-$$

The initial equilibrium has been investigated [9,10] and shown, by isotopic analysis, to be reached very rapidly compared with the hydrolysis—an essential factor in the proposed mechanism. The breakdown of CCl_3^- to CCl_2 appears, in the light of available evidence, to be the most probable second step. Carbon dichloride can then react rapidly to give carbon monoxide or formate ion. The specific salt effects obtained by adding chloride ion and iodide ion to the reactants are readily explained in terms of this mechanism. The reversal of stage (2) would result in a slowing down of the reaction, and in the case of iodide ion the formation of some trichloroiodomethane would account for the gradual increase of the rate constant with time, for this is hydrolysed more rapidly than chloroform.

Further evidence that carbon dichloride is an active intermediate has been obtained by Hine *et al.*[5-7] who have shown that several reactions of chloroform are strongly base-catalysed. In this work iodide–chlorine exchange into chloroform is shown to be strongly base-catalysed. Woodworth and Skell [11] have added carbon dichloride and carbon dibromide to buta-1 : 3-diene, showing that addition is of a three-centre type thus emphasising the electron-deficient character of the species. Wynberg [12] has also discussed carbon dichloride in the Reimer–Tiemann reaction.

If the mechanism for the alkaline hydrolysis of chloroform is as follows:

$$(1)\quad CHCl_3 + OH^- \underset{k_1}{\overset{k_2}{\rightleftharpoons}} CCl_3^- + H_2O$$

$$(2)\quad CCl_3^- \xrightarrow{k_3} Cl^- + CCl_2$$

$$(3)\quad CCl_2 + 2OH^- \longrightarrow CO + 2Cl^- + H_2O$$

$$(4)\quad CCl_2 + 3OH^- + H_2O \longrightarrow H{\cdot}CO{\cdot}O^- + 2Cl^- + 2H_2O$$

where reaction (2) is the rate-determining step, and reactions (3) and (4) are rapid, the rate of production of chloride ion is:

$$d[Cl^-]/dt = [k_2k_3/(k_1 + k_3)][CHCl_3][OH^-]$$

[6] Hine and Dowell, *J. Amer. Chem. Soc.*, 1954, **76**, 2688.
[7] Hine, Dowell, and Singley, *ibid.*, 1956, **78**, 479.
[8] Hine, Burske, Hine, and Langford, *ibid.*, 1957, **79**, 1406.
[9] Horiuti and Tanabe, *Proc. Japan Acad.*, 1951, **27**, 404; 1952, **28**, 127.
[10] Hine and Oaks, *J. Amer. Chem. Soc.*, 1954, **76**, 827.
[11] Woodworth and Skell, *ibid.*, 1957, **79**, 2542.
[12] Wynberg, *ibid.*, 1954, **76**, 4998.

The observed bimolecular constant is thus, not a unitary constant, but a unimolecular constant multiplied by what approximates to an equilibrium constant. This can account for the very high pre-exponential term (10^{16}) obtained in the Arrhenius equation. The decrease in the activation energy with increase in temperature, a most unusual feature for a reaction between an ion and a polar molecule,[13] can also be accounted for if the rate-determining step is a unimolecular reaction. The value for $\delta E_A/\delta T$ obtained in the alkaline hydrolysis of chloroform is higher even than that obtained in the acid hydrolysis (−133 and −92 cal./deg., respectively). This suggests that, in classical terms, the number of simple harmonic oscillators contributing to the decrease in activation energy with temperature of the first-order breakdown of the solvated CCl_3^- ion is higher than the number operating in the first-order breakdown of the solvated chloroform molecule. This could be explained in terms of the effect of the charge on solvation, but the increased value of $\delta E_A/\delta T$ may be complicated by a temperature effect on the equilibrium constant K.

Kinetics of the Hydrolysis of Carbon Tetrachloride

(a) *Hydrolysis of Carbon Tetrachloride in Water.*—This hydrolysis has been investigated in the temperature range 343—373° K, which is determined by the low solubility of carbon tetrachloride at the upper limit and the slowness of its reaction at the lower limit.

Experimental. Solutions for kinetic runs were prepared by injecting a measured volume of pure carbon tetrachloride from a 1 ml. glass syringe into a known volume of outgassed conductivity water. The concentration of carbon tetrachloride used was ~2 mmoles (max. 2·5). The reactions were carried out in the vapour-free, thermostat-controlled, Pyrex reaction vessel described on p. 400.

Reagents. Carbon tetrachloride ("AnalaR," Harrington Bros.) was treated in the same way as methylene dichloride.[2] On distillation the fraction of b. p. 76·70—76·80° (corr.) was collected (lit.,[3] b. p. 76·75°). Analysis by vapour-phase chromatography showed that less than 0·01% of other chlorinated methanes were present.

All solutions for kinetic runs were made up with conductivity water as above.

Analysis. The products of the hydrolysis are carbon dioxide and hydrogen chloride. The suggestion that hypochlorous acid is one of the products has been disproved, since no trace of the acid could be detected. Hydrogen ion and chloride ion were estimated by the methods previously described. Since the solutions used in the investigation were very dilute, uniformly illuminated backgrounds, carefully standardised techniques, and accurately calibrated, grade A, microburettes and pipettes were essential. The initial concentrations of solutions were checked by complete hydrolysis and chloride-ion analysis, using the sealed ampoule technique. The hydrolysing solution used was 4N-KOH in methanol–water (1 : 9 v/v).[14] The reaction has been established as $CCl_4 + 2H_2O \longrightarrow CO_2 + 4HCl$.

Kinetic analysis and results. The hydrolysis of carbon tetrachloride in water does not follow a first-order law. As this result was unexpected, some effort was made to reconcile the results with a first-order law. Careful examination of a series of runs at the same temperature with different concentrations of carbon tetrachloride showed that the reaction was of second order with respect to carbon tetrachloride. The results have therefore been calculated by using the equation $k_2 = (1/t)x/(a - x)$, where a is the concentration of carbon tetrachloride initially and $a - x$ that after time t. Values of k_2 are obtained graphically. Since the concentrations of hydrogen ion and chloride ion follow each other precisely within the limits of accuracy of the methods employed, the chloride-ion values are used in calculating k_2 as they are the more accurate. The results for a specimen run are given in Table 6. The ratio $t_{\frac{1}{2}} : t_{\frac{1}{3}} : t_{\frac{1}{4}}$ was found to be $1 : \frac{1}{3} : \frac{1}{7}$ in all cases, emphasising the second-order character of the kinetics. Table 7 gives the variation of the half-life with concentration for three runs at 373·16° K. Again the reaction is shown to be of second order with respect to carbon tetrachloride.

[13] Hurst, Thesis, Cambridge, 1948.
[14] Matchett, *J. Assoc. Off. Agric. Chem.*, 1929, **12**, 264.

TABLE 6. *Acid hydrolysis of carbon tetrachloride at* 373·16° K.

$10^3k_2 = 1{\cdot}208 \pm 0{\cdot}027$ l. mole^{-1} sec.$^{-1}$.

Time (min.)	$[Cl^-]$ (mmoles/l.)	x, obs.	x, calc.	Time (min.)	$[Cl^-]$ (mmoles/l.)	x, obs.	x, calc.
0	0	0	0	11,447	1·512	0·378	0·377
2,840	0·626	0·156	0·136	13,002	1·667	0·417	0·405
5,788	0·890	0·220	0·240	15,770	1·808	0·452	0·448
8,565	1·342	0·336	0·315	∞	3·612	0·903	0·903

$t_{1/2} = 15{,}870$ min.; $t_{1/4} = 5200$ min.; $t_{1/8} = 2150$ min.; $t_{1/2} : t_{1/4} : t_{1/8} = 1 : 1/3 : 1/7{\cdot}3$

TABLE 7.

$[CCl_4]$ (mmoles/l.)	$t_{1/2}$ (min.)	10^3k_2 (l./mole^{-1} sec.$^{-1}$)	$[CCl_4]$ (mmoles/l.)	$t_{1/2}$ (min.)	10^3k_2 (l./mole^{-1} sec.$^{-1}$)
0·903	15,870	$1{\cdot}208 \pm 0{\cdot}027$	2·261	4,850	$1{\cdot}592 \pm 0{\cdot}045$
1·465	8,870	$1{\cdot}258 \pm 0{\cdot}031$			

The results obtained experimentally conform, within the limits of the experimental accuracy, to the equation:

$$\log_{10} k_2 = 11{\cdot}0189 - 23{,}646/2{\cdot}303RT \quad . \quad . \quad . \quad . \quad . \quad - \quad (3)$$

The apparent energy of activation is probably correct to $\pm 1{\cdot}0$ kcal. The rate constants obtained experimentally show a slight decrease with decrease in initial concentration of carbon tetrachloride. Equation (3) refers to an initial concentration of 2·00 mmoles/l. of carbon tetrachloride. A comparison of the observed values of k_2 and those reproduced by equation (3) is given in Table 8. The observed values of k_2 are correct to $\pm 5\%$.

TABLE 8.

T (K)	10^3k_2, obs. (l./mole^{-1} sec.$^{-1}$)	$[CCl_4]_0$ (mmoles/l.)	10^3k_2 corr.	10^3k_2 calc.
343·14°	8·416	2·00	8·416	8·415
353·38	32·83	2·52	30·11	24·90
363·28	55·40	2·07	54·65	62·38
373·16	159·2	2·261	151·8	148·4
373·16	125·8	1·465	151·8	148·4
373·16	120·8	0·903	151·8	148·4

(b) *Kinetics of the Reaction between Carbon Tetrachloride and Dilute Aqueous Potassium Hydroxide.*—The kinetics of the hydrolysis of carbon tetrachloride in alkaline solution have been examined, different concentrations of potassium hydroxide being used, at 363° and 373° K, but, up to 0·08N, it has no effect on the rate of hydrolysis of the carbon tetrachloride, the rate being the same as that in pure water.

Experimental. The apparatus and techniques used to follow the reaction were the same as those described in part (*a*) of this section.

Analysis. Chloride ion was estimated by the modified Mohr's method; hydroxide ion was estimated by using standard nitric acid with Bromothymol Blue as indicator and nitrogen bubbling through the solution.

Kinetic analysis and results. As potassium hydroxide appears to have no effect on the rate of hydrolysis of carbon tetrachloride in aqueous solution, the kinetic analysis used is the same as that used in the acid hydrolysis of carbon tetrachloride; the bimolecular rate constants so obtained can then be compared with those obtained in pure water. The results of a specimen run are given in Table 9.

Similar runs were carried out at 363° and 373° K in solutions up to 0·08N in potassium hydroxide. The bimolecular rate constants obtained were identical with those obtained for the hydrolysis in pure water. 0·008N-Potassium chloride also had no effect on the rate of hydrolysis of carbon tetrachloride.

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TABLE 9. *Alkaline hydrolysis of carbon tetrachloride at* 373·16° K. (Concentrations in mmoles/l.)

$10^3k_2 = 1{\cdot}515 \pm 0{\cdot}030$ l. mole^{-1} sec.$^{-1}$.

Time (min.)	[Cl$^-$]	[KOH]	x, obs.	x, calc.
0	0	27·06	0	0
213	0·735	26·17	0·184	0·107
1429	2·20	24·90	0·550	0·570
2958	3·84	23·48	0·960	0·942
4278	4·34	22·50	1·085	1·158
5695	5·74	21·45	1·435	1·329
7129	5·82	21·16	1·455	1·461
∞	9·60	—	2·40	2·40

$t_{1/2} = 4400$ min.; $t_{1/4} = 1500$ min.; $t_{1/8} = 600$ min.; $t_{1/2} : t_{1/4} : t_{1/8} = 1 : 1/2{\cdot}95 : 1/7{\cdot}3$

Discussion.—The hydrolysis of carbon tetrachloride in neutral and acidic solutions does not conform to the general pattern displayed by the other members of the chlorinated methane series. The reaction appears to be bimolecular with respect to carbon tetrachloride and the values of k_2 obtained experimentally at different temperatures can be represented by an Arrhenius equation. If the rate of hydrolysis of carbon tetrachloride is compared with that for methylene dichloride on the basis of the half-lives of the reactions, using a concentration of 2 mmoles/l. for carbon tetrachloride, the rate for carbon tetrachloride is four times that for methylene dichloride.

The presence of potassium hydroxide in concentrations up to 0·08N has no detectable effect upon the rate of hydrolysis of carbon tetrachloride, the rate being the same as in pure solvent. If the reaction is carried out in 10% methyl alcohol the rate is increased fourfold. The rate of hydrolysis of carbon tetrachloride in water appears to be unaffected by the presence of potassium chloride in a concentration four times that of carbon tetrachloride.

A survey of the literature reveals conflicting results for the rate and mechanism of the hydrolysis of carbon tetrachloride. The confusion results from the comparison of work using different solvents and the neglect of the reaction between carbon tetrachloride and the solvent.

The following reactions have been reported. Hydrolysis in alcoholic potassium hydroxide gives carbon monoxide, ethyl orthoformate, and, under more dilute conditions, chloroform.[15] In water, carbon dioxide and hydrochloric acid are formed.[16] With excess of carbon tetrachloride it is claimed that carbonyl chloride is formed.[17] Qualitatively inexplicable results have been reported by Hine *et al.*[8] Anomalous isotopic-exchange reactions of carbon tetrachloride have also been reported.[18] It is thus clear that, when carbon tetrachloride is subjected to hydrolysis, the mechanism and products depend on the solvent.

Under the conditions of the present experiments, the products of hydrolysis are carbon dioxide and hydrochloric acid with no trace of hypochlorous acid, formic acid, or carbon monoxide. The reaction in pure water can be represented by the equation $CCl_4 + 2H_2O \longrightarrow CO_2 + 4HCl$, and the rate of the reaction is of the second order with respect to carbon tetrachloride. The reaction is found to go to completion in aqueous solution: the change in standard free energy is −90,000 cal. The reaction may proceed *via* an intermediate $CCl_3{\cdot}OH$ which breaks down rapidly to carbonyl chloride and then to carbon dioxide and hydrochloric acid. Like the reaction intermediates postulated in the acid hydrolysis of the other chlorinated methane, $CCl_3{\cdot}OH$ is probably unstable. Carbonyl chloride is known to react very rapidly with water,[19] the reaction being complete in less

[16] Turner and Harris, " Organic Chemistry," Longmans, Green and Co., London, 1952, p. 162.
[18] Benrath, *Annalen*, 1911, **382**, 223.
[17] Goldschmidt, *Ber.*, 1881, **14**, 928.
[18] Neyman, Miller, and Shapavalov, *J. Phys. Chem. U.S.S.R.*, 1955, **29**, 1042.
[19] Vles, *Rev. Trav. chim.*, 1934, **53**, 962.

than 60 sec. at 0°. Further evidence for the production of carbonyl chloride as an intermediate in this reaction is furnished by Goldschmidt, who obtained it when hydrolysing excess of carbon tetrachloride in water.

The bimolecular nature of the reaction with respect to carbon tetrachloride seems to indicate that the carbon tetrachloride molecule cannot directly interact with, or acquire energy from, water molecules. If the solvent is inert in this respect the bimolecular nature of the reaction can be explained by using Christiansen and Kramer's [20] formulation of the so-called Lindemann [21] effect in gaseous reactions at fairly low pressures. It is only necessary to postulate that a molecule of carbon tetrachloride can only be activated or deactivated by collision with another molecule of its own kind. The concentrations of carbon tetrachloride used in this investigation correspond to pressures in the range 20—50 mm. Hg, which is the range in which first-order characteristics of certain gas reactions give place to those of the second order.

The numerical value of the pre-exponential term in the Arrhenius equation supports inert-solvent interpretation, and is consistent with a simple collision process between solute molecules having an effective collision diameter of 3·72 Å. It is conceivable that the inert behaviour of water molecules towards carbon tetrachloride is connected with the absence of the C–H bond. The first three members of the chlorinated methane series have a common vibration frequency of about 3040 $cm.^{-1}$, which is attributable to C–H bonds. The fundamental vibration frequencies of water are 3652, 1595, and 3756 $cm.^{-1}$ and lie sufficiently close to the C–H value to make interaction likely. The carbon tetrachloride molecule has no vibration frequency which can be compared with those of the water molecule. The importance of the C–H group and its position in an ester molecule undergoing hydrogen-ion catalysed hydrolysis has been discussed by Moelwyn-Hughes.[22]

The very different hydrolysis rates found when organic molecules such as methyl alcohol are introduced into the carbon tetrachloride–water system may well be due to the presence of C–H bonds in the mixed solvents. The pollution of aqueous solutions by methanol or ethanol certainly simplifies manipulation by ensuring a much higher solubility, but it does not simplify the chemistry of the reactions.

Carbon tetrachloride, as the last member of the chlorinated methane series, probably reacts by a rate-determining ionic mechanism rather than the " bimolecular " mechanism of the other three members of the series. The absence of any difference in rate of hydrolysis in water or 0·08N-potassium hydroxide shows clearly that the rate-determining step is a breakdown of the carbon tetrachloride molecule followed by reaction with either water or hydroxide ion.

The alternative mechanism leading to products of hydrolysis such as chloroform, carbon monoxide, formate, etc., is presumably the result of performing the reaction in a solvent which is less ionising than water. Under these conditions attack by hydroxide ion on the non-polar, heavily chlorinated carbon tetrachloride molecule could give hypochlorous acid and the CCl_3^- ion, resulting in a rapid reaction with hydroxide ion giving products similar to those obtained in the alkaline hydrolysis of chloroform.

General Discussion

The experimental study of the hydrolysis and substitution reactions of the halogenomethanes was undertaken in the hope that the effect of substitution on their rates could be interpreted theoretically. There are many theories on the kinetics and mechanisms of such reactions. The theories of organic chemistry, such as those developed by Ingold [23] and his collaborators, interpret the effect of substituting one atom for another in terms of the drift of electrons towards or away from the seat of attack. The theories of physical

[20] Christiansen and Kramer, *Z. phys. Chem.*, 1923, **103**, 91.
[21] Lindemann, *Trans. Faraday Soc.*, 1922, **17**, 599.
[22] Moelwyn-Hughes, " Kinetics of Reactions in Solution," 2nd Ed., Oxford, 1947, p. 336.
[23] Ingold, " Structure and Mechanism in Organic Chemistry," Bell and Sons Ltd., London, 1953.

chemistry include an attempt to interpret rates of reactions in terms of intermolecular forces,[1] particularly those of electrostatic origin, and to evaluate the absolute limiting heat content of reactive solutes.[2] Such theories, though naturally differing in approach and emphasis, are complementary rather than contradictory. Moreover, they have at least one feature in common; while each is capable of providing a logical basis for discussing the effects of substitution in a series of reactions proceeding by a common mechanism, neither is capable of predicting at what stage in any series a postulated mechanism breaks down, to be replaced by one that is quite different. In this respect they resemble the most advanced theories of simple gas reactions. While Heitler and London's theory of the mutual conversion of covalent bonds allows an evaluation of the energy of activation, as Eyring and Polanyi in particular have shown, it can interpret but not predict the fact that hydrogen and iodine react by a molecular mechanism while hydrogen and bromine react by an atomic mechanism. The completely unexpected change of mechanism evinced by the molecules CH_3Cl, CH_2Cl_2, $CHCl_3$, and CCl_4 in simple reactions in solution exposes the inadequacy of all theories hitherto advanced on the kinetics of reactions in solution.

Methyl chloride, the first member of the series, is hydrolysed in pure water at a constant pressure, and in the absence of the vapour phase, by a reaction which is of the first order with respect to the solute, and of a high but undetermined order with respect to the solvent. The energy of activation decreases as the temperature is raised, until it reaches either a limiting or a minimum value. No equation has been found to represent the variation of the velocity constant with respect to temperature. The reaction between methyl chloride and the hydroxyl ion is ostensibly simpler, being of second order, and not unlike substitution reactions of the same class in various solvents. The second member of the series, methylene dichloride, kinetically resembles the first member in many respects. The pseudo-unimolecular constant governing its reaction with the solvent increases with temperature in such a way as to indicate a decrease in the value of the activation energy as the temperature is raised. In alkaline solution, each molecule of methylene dichloride reacts with two hydroxyl ions, yielding formaldehyde, but the reaction is of the second and not the third order. The mechanism of the substitution seems not to have changed, except that the first substitution is followed by a further and relatively rapid one. The numerical value of the second-order constant is only 1/150 of the value for methyl chloride, the reduction in rate being attributable in nearly equal measure to a lowering in the A term and an increase in the E_A term of the Arrhenius equation $k_2 = A \exp(-E_A/RT)$. There are also subsequent chemical changes, including the Cannizzaro reaction, which can be allowed for or eliminated. As far as its reaction with the pure solvent is concerned, the third member, chloroform, does not differ markedly from the first two members, except that the rate is slower and the energy of activation, as well as its rate of decrease with temperature, is higher. It is in its reaction with the hydroxyl ion that anomalies appear. The second-order velocity constant is found to be 10 times as great as for methyl chloride and nearly 2000 times as great as for methylene dichloride. Moreover, log k_2 does not vary linearly with respect to $1/T$ but changes in a manner resembling that in pure hydrolysis. Some of these effects were not unexpected. On electrostatic grounds, one would expect the hydroxyl ion to approach the methyl chloride molecule from the carbon end of the C–Cl bond, and the chloroform molecule from the hydrogen end of the C–H bond. Collateral work by Hine *et al.*[5,6,7,8] suggests that the reaction involves the formation of labile intermediaries, such as the CCl_3^- ion and the CCl_2 radical, for the existence of which there is circumstantial evidence. The widest departure from a consistent behaviour is shown by the fourth member of the series, carbon tetrachloride, the rate of hydrolysis of which (to carbon dioxide and hydrochloric acid) is unaffected by hydroxyl ions, and is, as far as can be judged, a reaction of the second order, *i.e.*, the instantaneous rate of hydrolysis is proportional to the square of the concentration of carbon tetrachloride.

While no known theory can at present accommodate such a diversity of phenomena, the data for methyl chloride and methylene dichloride may profitably be compared with

one another and with those relating to other methyl halides in aqueous solution. It is clear from the data in Tables 10 and 11 that, although the rates of the various hydrolyses and of the substitution of the hydroxyl group into the various molecules differ by factors of several thousands, the constitutive effect on the velocity, whatever may be its origin, is similar in the hydrolytic and the substitutive reactions. Allowing for the extrapolation necessary to compare the first-order coefficients obtained at high temperatures with the second-order coefficients obtained at lower temperatures, we may regard the ratio k_2/k_1 as constant. Its average value from these data is 216, to within $\pm 27\%$. A rough value previously accepted [24] was 250. The constancy of this ratio indicates the similarity in the

TABLE 10. *Hydrolysis of halogenomethanes.*

Solute	k_1 at 373·16° K (sec.$^{-1}$)	Relative k_1	E_A at 373·16° K (kcal./mole)	k_2/k_1 (l. mole^{-1})
CH_2Cl_2	$5{\cdot}77 \times 10^{-7}$	1	26·5	279
CH_3F	$4{\cdot}35 \times 10^{-6}$	7·5	22·9	206
CH_3Cl	$1{\cdot}49 \times 10^{-4}$	260	26·3	162
CH_3Br	$1{\cdot}71 \times 10^{-3}$	3000	25·3	206
CH_3I	$5{\cdot}44 \times 10^{-4}$	940	26·3	228
CH_3NO_3	$2{\cdot}98 \times 10^{-5}$	52	26·3	—

TABLE 11. *Reactions of halogenomethanes with hydroxyl ion in water.*

Reaction	k_2 at 373·16° K (l. mole^{-1} sec.$^{-1}$)	Relative k_2	E_A at 373·16° K (kcal./mole)	$A \times 10^{10}$ (l. mole^{-1} sec.$^{-1}$)
$CH_2Cl_2 + OH^-$	$1{\cdot}61 \times 10^{-4}$	1	26·2	36·9
$CH_3F + OH^-$	$8{\cdot}98 \times 10^{-4}$	5·6	21·6	0·405
$CH_3Cl + OH^-$	$2{\cdot}42 \times 10^{-2}$	150	24·3	411
$CH_3Br + OH^-$	$3{\cdot}52 \times 10^{-1}$	2200	23·0	1040
$CH_3I + OH^-$	$1{\cdot}24 \times 10^{-1}$	770	22·2	124

reactions (1) $RX + H_2O \longrightarrow ROH + HX$ and (2) $RX + OH^- \longrightarrow ROH + X^-$. It is conceivable that reaction (2), like (1), is in fact a hydrolysis, differing from reaction (1) only in that the water molecule reacting is brought to the sphere of action attached to a hydroxyl ion. Alternatively, reaction (1) may be an ionic substitution, differing from reaction (2) only in that the hydroxyl ion is generated from one of the water molecules surrounding RX.

The chemical change during hydrolysis of the methyl halides may be represented as:

$$CH_3X + \nu H_2O \longrightarrow CH_3{\cdot}OH + [H,\nu_+H_2O]^+ + [X,\nu_-H_2O]^-$$

where ν stands for the order of reaction with respect to water, and ν_+ and ν_- are the respective co-ordination numbers of the cation and anion formed.

The rate-determining step is thought to be the simultaneous attack of the solute molecule by a number, ν, of the solvent molecules which surround it. The evidence for accepting this view is that substituted methyl halides do not react with steam at temperatures where hydrolysis in water is extremely rapid, and that the rate of fall of the activation energy with respect to temperature is greater than can be accounted for unless a number of water molecules participate in the activation.[25] Indirect evidence is the similarity between the values of $\delta E_A/\delta T$ for the first three members of the series and the values of ΔC_p given by Glew and Moelwyn-Hughes [26] for the process of escape of these chloromethane vapours from water. If it is assumed that only two of the three vibration frequencies of water are active in both dissolution and hydrolysis, it appears that most of the water molecules in the solvating shell take part in the hydrolysis.

The rate of hydrolysis may then be written as $-dn/dt = k_w \cdot n \cdot n_w^{\nu}$, where n is the

[24] Moelwyn-Hughes, *op. cit.*, ref. 22, p. 80.
[25] *Idem*, *Proc. Roy. Soc.*, 1938, *A*, **164**, 295.
[26] Glew and Moelwyn-Hughes, *Discuss. Faraday Soc.*, 1953, **15**, 150.

concentration of methyl halide and n_w is that of water; ν is the number of water molecules taking part in the activation process.

In the reactions of the methyl halides with the hydroxide ion a similar mechanism may well prevail, the solvating water molecules again playing a significant rôle in the reaction. The rate of reaction would then be

$$-\mathrm{d}n/\mathrm{d}t = k_s \,.\, n[n_w - \sum n_i\nu_i]^p n_{OH}\text{-}[n_w - \sum n_i\nu_i]^q$$

The term in square brackets denotes the concentration of free water molecules in terms of the total, formal concentration of water, n_w, and the concentrations of the ions. Effectively the term is n_w so that:

$$k_1 = k_w n_w{}^\nu \text{ and } k_2 = k_s n_w{}^{p+q}$$

where $p + q$ is the number of water molecules taking part in the reaction between hydroxyl ion and methyl halide. The ratio k_1/k_2 thus depends on k_s/k_w and on the numbers ν, p, and q. As the numbers of oscillators contributing to the activation energy in the systems are not known accurately, a more precise formulation is not possible. The fact that the variation of k_2 with respect to temperature conforms to the simple equation of Arrhenius suggests that the reaction with hydroxide ion is in some way simpler than the solvolysis. It is possible that the hydroxide-ion attack on the halide molecule is brought about by a proton-transfer mechanism through the solvating shells of the reactants, causing ionisation of one of the solvating water molecules adjacent to the halide molecule. Such a mechanism can account for the simplification in the energetics of the system, and is, of course, restricted to reactions between un-ionised solutes and one of the ions into which the solvent can ionise.

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73. *The Synthesis of* 1-*Glycosylbenziminazoles.*

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Methods for the synthesis of 1-D-galactosyl- and 1-(2-deoxy-D-galactosyl)-benziminazole have been compared. Best results are obtained from the direct condensation in dry dioxan of the *O*-acetylglycosyl halide and benziminazole and deacetylation of the product by the Zemplén procedure. A series of compounds of this class has been synthesised and examined for bacteriostatic action against *E. coli* 15. The stability of some of the compounds in 6N-hydrochloric acid at 100° and 150° has been investigated. It is less if a deoxy-group is present in the sugar moiety.

In connexion with an investigation of certain anti-metabolites, a series of glycosylbenziminazoles was required. Two main methods are available for the synthesis of 1-glycosylbenziminazoles. Either a mono-*N*-glycosyl derivative of *o*-phenylenediamine can be converted into a benziminazole derivative,[1-5] or a suitable benziminazole derivative can be condensed with an *O*-acetylglycosyl halide.[4-9] These methods have been examined for the preparation of 1-β-D-galactopyranosylbenziminazole in reasonable yield.

[1] Brink, Holly, Shunk, Peel, Cahill, and Folkers, *J. Amer. Chem. Soc.*, 1950, **72**, 1866.
[2] Holly, Shunk, Peel, Cahill, Lavigne, and Folkers, *ibid.*, 1952, **74**, 4521.
[3] Buchanan, Johnson, Mills, and Todd, *J.*, 1950, 2845.
[4] Cooley, Ellis, Mamalis, Petrow, and Sturgeon, *J. Pharm. Pharmacol.*, 1950, **2**, 579.
[5] Mamalis, Petrow, and Sturgeon, *ibid.*, 1950, **2**, 491, 503, 512.
[6] Weygand, Wacker, and Wirth, *Z. Naturforsch.*, 1951, **6**b, 25.
[7] Davoll and Brown, *J. Amer. Chem. Soc.*, 1951, **73**, 5781.
[8] Johnson, Miller, Mills, and Todd, *J.*, 1953, 3061.
[9] Heyl, Chase, Shunk, Moore, Emerson, and Folkers, *J. Amer. Chem. Soc.*, 1954, **76**, 1355.

2 : 3 : 4 : 6-Tetra-*O*-acetyl-α-D-galactosyl bromide, condensed with benziminazolylsilver, gave a dark product from which crystalline 1-β-D-galactosylbenziminazole was isolated (overall yield 17·2%) after chromatography to remove unchanged benziminazole and deacetylation. The compound was smoothly oxidised by 2 mol. of sodium periodate with the liberation of 1 mol. of formic acid, which showed it to be a pyranoside. The β-configuration was assigned on the assumption that a Walden inversion occurred during the condensation. In all experiments with this procedure considerable decomposition occurred. Although lowering the temperature prevented this, it also slowed the reaction and so improved yields were not obtained. An excess of vigorously stirred finely divided benziminazolylsilver should be used since it becomes coated with silver bromide as the reaction proceeds: this slows the reaction. Deacetylation of the crude product by the Zemplén–Pacsu method [10] was satisfactory and the objections to the method mentioned by Mamalis *et al.*[5] were not encountered. These workers and also Johnson *et al.*[8] used boiling mineral acid to deacetylate similar compounds: the stability of the *N*-glycosyl linkage apparently precludes hydrolysis but it has now been shown (see below) that in some cases isomerisation can occur and for this reason the Zemplén deacetylation method is preferable.

Condensing tetra-*O*-acetyl-α-D-galactosyl bromide with chloromercuribenziminazole in boiling xylene (cf. Davoll and Brown [7]) followed by deacetylation gave a slightly better yield (23%) of the galactosylbenziminazole. [The chloromercuribenziminazole was made by the addition of a solution of benziminazole and sodium hydroxide to one of mercuric chloride instead of *vice versa*, to prevent the formation of dibenziminazolylmercury, which apparently was a contaminant in Davoll and Brown's product.[7]] The best method of synthesis was to heat tetra-*O*-acetyl-α-D-galactosyl bromide with an excess of benziminazole in dry dioxan. After deacetylation 1-β-D-galactosylbenziminazole was obtained in 37% overall yield. Undesired side-reactions undoubtedly occur, probably base-catalysed reactions leading to products of the *O*-acetylglycoseen and the *O*-acetyl-1 : 6-anhydroglycose type. This method has been employed by Johnson *et al.*[8] to give acetylated glycosylbenziminazoles but was developed independently in the present work which was completed in 1953 [11] before the publication by Johnson *et al.*[8] An attempt to condense the galactosyl halide with benziminazole at room temperature using the improved Koenigs–Knorr technique [12] was unsuccessful, as was an attempt to prepare 1-β-D-galactosylbenziminazole by cyclisation of the appropriate *N*-glycosyl-*o*-phenylenediamine with ethyl orthoformate. 1-β-D-Galactosylbenziminazole gave a glassy tetra-acetate and solid 6-*O*-triphenylmethyl and 3 : 4(?)-*O*-*iso*propylidene derivatives. As the latter compound was prepared by treating the glycosylamine with acetone and acid it is not certain that the β-configuration is retained (see p. 411).

To synthesise 1-(2-deoxy-D-hexosyl)benziminazoles, acetohalogeno-2-deoxyhexoses are required as intermediates. The method of preparation adopted was to add hydrogen halide to an acetylated glycal in benzene containing benzoyl peroxide. In this way a crude tri-*O*-acetyl-2-deoxy-D-galactosyl bromide was synthesised from tri-*O*-acetyl-D-galactal. Treatment with aniline and subsequent deacetylation yielded 2-deoxy-*N*-phenyl-D-galactosylamine. Condensing the crude bromide with benziminazolylsilver in xylene gave after deacetylation a lævorotatory form (*A*) of 1-(2-deoxy-D-galactosyl)-benziminazole (14%), also obtained (in 5% yield) by using chloromercuribenziminazole instead of benziminazolylsilver. Treatment of the acetyldeoxygalactosyl bromide with an excess of benziminazole in dioxan at 100° yielded a small amount of the above lævorotatory compound together with more (30%) of a dextrorotatory isomer (*B*). The formation of two isomers, which are probably α- and β-forms, is not surprising in view of the syrupy nature of the *O*-acetylglycosyl halide employed, but it is not clear why isomer (*B*) should be the

[10] Zemplén and Pacsu, *Ber.*, 1929, **62**, 1613.
[11] Cleaver, Final Report to D.S.I.R., 1953.
[12] Reynolds and Evans, *J. Amer. Chem. Soc.*, 1938, **60**, 2559.

main product of condensation with benziminazole whereas isomer (*A*) is the main product from salts of the base. Isomer (*B*) was converted into (*A*) by boiling dilute mineral acid and as far as the authors are aware this is the first time that interconversion of α- and β-forms of sugars attached to a tertiary nitrogen atom has been observed. Several derivatives of these compounds were prepared. A syrupy triacetate of isomer (*B*) yielded a crystalline picrate which could be used as a means of isolating and purifying the condensation product of tri-*O*-acetyl-2-deoxy-D-galactosyl bromide and benziminazolylsilver. Two crystalline mono*iso*propylidene derivatives of 1-(2-deoxy-D-galactosyl)benziminazole (*A*) were isolated, both of which gave correct analyses and were hydrolysed rapidly by dilute hydrochloric acid at 100° to the initial material (*A*). These derivatives are probably also α- and β-forms although the possibility that the *iso*propylidene residue is linked in different positions (*e.g.*, 3 : 4 and 4 : 6) cannot be excluded. That 1-(2-deoxy-D-galactosyl)-benziminazole (*B*) is isomerised by 0·01N-hydrochloric acid would account for the formation of (*A*) on hydrolysis of both *iso*propylidene derivatives.

1-(2 : 6-Dideoxy-D-galactosyl)benziminazole was synthesised as follows: D-galactose was converted into D-fucose from which 3 : 4-di-*O*-acetyl-D-fucal (3 : 4-di-*O*-acetyl-6-deoxy-D-galactal) was prepared. When treated with hydrogen chloride in dry benzene this afforded 3 : 4-di-*O*-acetyl-2 : 6-dideoxy-D-galactosyl chloride which was condensed in the crude state with benziminazolylsilver to give 1-(di-*O*-acetyl-2 : 6-dideoxy-D-galactosyl)-benziminazole, which was then deacetylated. 1-(Di-*O*-acetyl-2-deoxy-L-ribosyl)benziminazole picrate [4] and 1-(2-deoxy-L-ribosyl)benziminazole were prepared likewise. The latter compound slowly gave a blue colour with the Dische reagent,[13] indicating that slow hydrolysis occurred under the hot strongly acid conditions of this colour test. Cooley *et al.*[4] prepared a 1-(di-*O*-acetyl-2-deoxy-D-ribosyl)benziminazole which differs in melting point but has the same sign for its optical rotation as our product. It is probable that the two compounds have different glycosidic configurations (cf. results of Davoll and Lythgoe [14] who obtained two isomeric 2-deoxyribosides by condensing di-*O*-acetyl-2-deoxy-D-ribosyl chloride with theophyllinylsilver).

1-(2-Deoxy-D-glucosyl)benziminazole was also prepared.

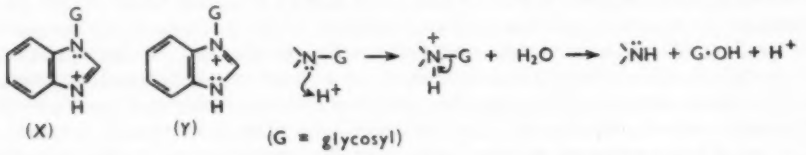
In addition to various glycosyl derivatives of benziminazole, the corresponding D-galactosyl and 2-deoxy-D-galactosyl derivatives of 5 : 6-dimethylbenziminazole were prepared.

The stability of some of the 1-glycosylbenziminazoles in 6N-hydrochloric acid was examined chromatographically. 1-β-D-Galactosylbenziminazole (*a*), 1-(2-deoxy-D-galactosyl)benziminazole (*b*), and 1-(2 : 6-dideoxy-D-galactosyl)benziminazole (*c*) were separately heated in the acid at 100° and 150°. The results of the chromatographic analysis of the products are shown in the Experimental section. Although the compounds are glycosylamines they are very resistant. Introduction of the 2-deoxy-group increases the lability and this is accentuated in the 2 : 6-dideoxy-derivative. This is a further example of the greater lability of 2-deoxyhexosides than of hexosides. Cooley *et al.*[4] showed a similar relation for 5 : 6-dimethylbenziminazole pentose and deoxypentose derivatives. It is of interest that the isomerisation mentioned previously was encountered for the glycosides of a 2-deoxy-sugar. The acid-stability of 1-glycosylbenziminazoles may be due to the existence in acid solution of compounds of this class as substituted benziminazolium ions, the positive charge being distributed throughout the ring system.

Structures (*X*) and (*Y*) would be expected to be the main contributors although the resonance energy will not be so great as in the unsubstituted benziminazolium ion where the two main contributors to the system are identical. The contribution made by (*Y*) effectively places a fractional positive charge on $N_{(1)}$. This will tend to prevent protonation at this site, which is a primary step in the acid hydrolysis of these compounds and which can be depicted as shown. Introduction of a 2-deoxy-group will lower the $-I$

[13] Dische, *Mikrochemie*, 1930, **8**, 4.
[14] Davoll and Lythgoe, *J.*, 1949, 2526.

effect of the glycosyl residue, assisting in the splitting of the $\geq C-N<$ linkage. In addition certain stereochemical factors will be operative which will assist the hydrolysis.[15] It is interesting to contrast the acid-stability of 1-glycosylbenziminazoles with the acid-lability of 9-glycosylpurines. In the latter type of compound the positive charge can be



partly accommodated on the nitrogen atoms of the six-membered ring and so protonation of the glycosylated nitrogen atom is not effectively prevented as in the glycosylbenziminazoles. We should note Kenner's ideas [16] on this problem and work is in progress to obtain further evidence.

A series of benziminazole derivatives were tested for bacteriostatic action on *E. coli* 15 (see p. 417).

Experimental

Benziminazolylsilver.—Phillips's procedure [17] was modified as follows: To a stirred solution of benziminazole (11·8 g.) in water (500 c.c.) at 95° an aqueous solution of silver nitrate (17 g. in 80 c.c.) and aqueous ammonia (20 c.c.; *d* 0·880) were added slowly. After 0·5 hr. the white precipitate was collected, washed successively with boiling water, ethanol, and ether, and dried (21·8 g.). Before being used the product was finely pulverised and heated for 12 hr. at 115°.

5 : 6-Dimethylbenziminazolylsilver was prepared in almost identical fashion.

Chloromercuribenziminazole.—Davoll and Brown's method [7] was adapted. A solution of benziminazole (11·8 g.) and sodium hydroxide (4·0 g.) in hot 10% ethanol (1 l.) was added slowly to a stirred solution of mercuric chloride (27·2 g.) in ethanol (300 c.c.). The precipitate which separated on storage of the mixture was washed with water and dried (32 g.).

1-β-D-*Galactosylbenziminazole.*—(*a*) A mixture of benziminazolylsilver (21·9 g.) and xylene (500 c.c.) was distilled until 50 c.c. of distillate had been collected, then cooled. Powdered tetra-*O*-acetyl-α-D-galactosyl bromide (40 g.) was added, the distillation was repeated, and then the mixture was heated under reflux (moisture excluded) for 2 hr. and filtered. (Longer refluxing had no effect on the yield.) The residue was washed with hot xylene. On storage at 0° the combined filtrate and washings deposited crystalline benziminazole (2 g.), m. p. 173°. The xylene liquors were evaporated under diminished pressure to a black gum which was transferred in chloroform (50 c.c.) to an alumina column (40 × 3 cm.). The residue from evaporation of chloroform washings (400 c.c.) of the column was dissolved in dry methanol (200 c.c.) containing a trace of sodium methoxide. After 5 days solid material (5 g.) had crystallised. Further material was obtained from the mother-liquors by treatment with carbon dioxide and evaporation. Recrystallisation from water afforded 1-β-D-*galactosylbenziminazole* (4·7 g.), m. p. 257° (decomp.), $[\alpha]_D^{18}$ −31·5° (*c* 1·18 in C_5H_5N) (Found: C, 55·45; H, 5·8; N, 9·8. $C_{13}H_{16}O_5N_2$ requires C, 55·7; H, 5·75; N, 10·0%). The compound is soluble in hot water, hot ethanol, and pyridine. It does not give a Molisch test. The *picrate* crystallised from water as yellow needles, m. p. 169—170°, $[\alpha]_D^{19}$ −15·3° (*c* 1·05 in C_5H_5N) (Found: C, 44·4; H, 3·8; N, 13·75. $C_{12}H_{16}O_5N_2,C_6H_3O_7N_3$ requires C, 44·8; H, 3·8; N, 13·75%). The *hydrochloride monohydrate* had m. p. 197° (Found: C, 46·9; H, 5·6; N, 8·2; Cl, 10·9. $C_{13}H_{16}O_5N_2,HCl,H_2O$ requires C, 46·6; H, 5·7; N, 8·4; Cl, 10·6%). 1-β-D-Galactosylbenziminazole (0·0993 g.) consumed 2·04 mol. of sodium periodate in 240 min. and liberated 0·94 mol. of formic acid.

(*b*) A suspension of finely divided chloromercuribenziminazole (8·6 g.) in xylene (700 c.c.) was distilled (300 c.c. of distillate) and, after cooling, tetra-*O*-acetyl-α-D-galactosyl bromide (10 g.) was added and boiling was continued for 2 hr. (moisture excluded). The xylene was decanted and the brown residue was extracted with hot chloroform. The filtered extracts

[15] Foster and Overend, *Chem. and Ind.*, 1955, 566.
[16] Kenner, in "The Chemistry and Biology of Purines," London, J. & A. Churchill, Ltd., 1957, p. 312.
[17] Phillips, *J.*, 1931, 1143.

were evaporated under diminished pressure to 150 c.c. Successive washing with water (2 × 100 c.c.), 10% sodium iodide solution (3 × 100 c.c.), and water (3 × 100 c.c.), drying (Na_2SO_4), and evaporation afforded a material which was purified by passage through alumina and deacetylated as above. 1-β-D-Galactosylbenziminazole (1·56 g.) was obtained as prisms, m. p. 257° (decomp.), $[\alpha]_D^{19}$ −31·1° (*c* 1·09 in C_5H_5N).

(*c*) A solution of tetra-*O*-acetyl-α-D-galactosyl bromide (10 g.) and benziminazole (6·32 g.) in dry dioxan (25 c.c.) was heated at 100° for 0·5 hr. (moisture was excluded) and dry benzene (50 c.c.) was added to the cooled solution. A deposit of benziminazole mixed with its hydrobromide slowly separated and was collected and washed with benzene. From the washings and filtrate a brown syrup was isolated. In chloroform solution (100 c.c.) this was washed with 2N-ammonia (3 × 50 c.c.) and water (3 × 100 c.c.) and by the procedure described above 1-β-D-galactosylbenziminazole (2·5 g.), m. p. 257° (decomp.), $[\alpha]_D^{26}$ −31·5° (*c* 1·21 in C_5H_5N), was isolated.

An attempt was made to condense dry powdered benziminazole and tetra-*O*-acetyl-α-D-galactosyl bromide by an improved Koenigs–Knorr procedure. Benziminazole (2·87 g.), dry silver carbonate (6·7 g.), freshly ignited calcium sulphate (25 g.), and dry chloroform (50 c.c.) were stirred together for 1 hr. in the dark. After addition of iodine (1·25 g.) a solution of the acetylgalactosyl bromide (10 g.) in dry chloroform (40 cc.c.) was added dropwise during 1 hr. Stirring was continued for 24 hr. and the mixture was filtered through "Celite." Only unchanged benziminazole and tetra-*O*-acetyl-α-D-galactosyl bromide were isolated. The bromide was recovered quantitatively.

Acetylation (anhydride in pyridine) of the glycoside yielded 1-(2 : 3 : 4 : 6-*tetra*-O-*acetyl*-β-D-*galactosyl*)*benziminazole* as a colourless glass, $[\alpha]_D^{20}$ −17·6° (*c* 1·71 in $CHCl_3$) (Found: N, 6·3. $C_{21}H_{24}O_9N_2$ requires N, 6·25%).

1-(O-iso*Propylidene*-β-D-*galactosyl*)*benziminazole*.—To a swirled suspension of dry finely powdered 1-(β-D-galactosylbenziminazole) (2·0 g.) in dry acetone (120 c.c.) at 0° concentrated sulphuric acid (4·6 c.c.) was added dropwise. After 2 hr. at room temperature the cooled solution was added slowly to a stirred ice-cold solution of sodium carbonate (20 g.) in water (20 c.c.). After removal of the acetone at 50° the white solid remaining in suspension was filtered, washed with water, and dried. Recrystallisation from aqueous ethanol afforded the *mono*-O-iso*propylidene derivative* (1·1 g.) as prisms, m. p. 240—241° (decomp.), $[\alpha]_D^{22}$ +43·8° (*c* 0·914 in C_5H_5N) (Found: C, 60·2; H, 6·3; N, 9·0. $C_{16}H_{20}O_5N_2$ requires C, 60·0; H, 6·3; N, 8·75%).

1-(6-O-*Trityl*-β-D-*galactosyl*)*benziminazole*.—1-β-D-Galactosylbenziminazole (1 g.) was kept with triphenylmethyl chloride (0·973 g.) in pyridine (8 c.c.) at 100° for 6 hr. The product was isolated in standard fashion and the 6-O-*trityl derivative* (0·9 g.) was obtained as a granular white solid, m. p. 234° (decomp.), $[\alpha]_D^{22}$ −15·8° (*c* 1·01 in C_5H_5N) (Found: N, 5·1. $C_{32}H_{30}O_5N_2$ requires N, 5·4%).

Crude Tri-O-*acetyl*-2-*deoxy*-D-*galactosyl Bromide*.—Tri-*O*-acetyl-D-galactal (20 g.) and benzoyl peroxide (250 mg.) were dissolved in dry benzene (150 c.c.), and the solution was saturated at room temperature with dry hydrogen bromide. The solution was evaporated under reduced pressure at 30° and dry benzene was distilled in a vacuum over the residue. The product was a straw-coloured syrup which on storage decomposed with evolution of hydrogen bromide. The bromide (from 10·5 g. of tri-*O*-acetyl-D-galactal) was dissolved in dry ether (100 c.c.), and silver carbonate (10 g.) was added. To the stirred mixture aniline (4 c.c.) was added and after 12 hr. the product was isolated and deacetylated (Zemplén method). 2-Deoxy-*N*-phenyl-D-galactosylamine (2·1 g., 23% based on tri-*O*-acetyl-D-galactal) was obtained, having m. p. 130°, $[\alpha]_D^{15}$ −52·2° (equilibrium) (*c* 1·11 in MeOH). Butler *et al.*[18] give m. p. 134—135° and $[\alpha]_D^{18}$ −53° (*c* 1·3 in MeOH).

1-(2-*Deoxy*-D-*galactosyl*)*benziminazole*.—(*a*) The crude bromo-derivative (from 31·6 g. of tri-*O*-acetyl-D-galactal) in dry xylene (500 c.c.), and dry benziminazolylsilver (26·1 g.) were kept at 100—120° for 1 hr. Chloroform (100 c.c.) was added and after filtration the product was isolated and deacetylated as described for the corresponding galactosyl derivative. After recrystallisation from water 1-(2-*deoxy*-D-*galactosyl*)*benziminazole* (A) (4·3 g., 14%) was obtained as needles, m. p. 214°, $[\alpha]_D^{25}$ −18·9° (*c* 1·06 in C_5H_5N) (Found: C, 58·8; H, 6·4; N, 10·6. $C_{13}H_{16}O_4N_2$ requires C, 59·1; H, 6·1; N, 10·6%) {*picrate*, yellow needles (from water), m. p. 160°, $[\alpha]_D^{19}$ −9·07° (*c* 1·98 in C_5H_5N) (Found: C, 46·5; H, 3·8; N, 14·3. $C_{13}H_{16}O_4N_2,C_6H_3O_7N_3$

[18] Butler, Laland, Overend, and Stacey, *J.*, 1950, 1433.

requires C, 46·25; H, 3·9; N, 14·2%); *hydrochloride*, m. p. 152° (decomp.), $[\alpha]_D^{20}$ +5·17° (*c* 1·55 in H_2O) (Found: C, 51·8; H, 5·7; N, 9·6; Cl, 11·5. $C_{13}H_{16}O_4N_2$,HCl requires C, 51·9; H, 5·7; N, 9·4; Cl, 11·8%)}.

(*b*) The 1-bromo-derivative (from 11·7 g. of tri-*O*-acetyl-D-galactal) was added in a small volume of dry xylene to a suspension of chloromercuribenziminazole (15·2 g.) in xylene (400 c.c.), and the mixture was kept at 110—120° for 2 hr. Working up was as for the galactosyl analogue and 1-(2-deoxy-D-galactosyl)benziminazole (*A*) (0·57 g.), m. p. 214°, $[\alpha]_D^{20}$ −17·9° (*c* 1·12 in C_5H_5N), was obtained.

(*c*) Tri-*O*-acetyl-D-galactosyl bromide (from 10·2 g. of tri-*O*-acetyl-D-galactal) and dry powdered benziminazole (9·7 g.) were swirled for 1 hr. in dry dioxan at 100°. Dry benzene (100 c.c.) was added and after 12 hr. the precipitate (11·1 g.) was collected and washed with benzene. The combined filtrate and washings were evaporated to a syrup. In chloroform solution this was washed with 2N-ammonia (2 × 50 c.c.) and water (3 × 100 c.c.), dried (Na_2SO_4), evaporated to small bulk, and placed on an alumina column (24 × 3 cm.). The column was washed with chloroform (250 c.c.) and from the eluate a syrup was obtained which was deacetylated in dry methanol (200 c.c.) by the Zemplén procedure. Needles of 1-(*2-deoxy-D-galactosyl*)*benziminazole* (B) (2·92 g.), m. p. 199—200°, $[\alpha]_D^{22}$ +21·6° (*c* 1·11 in C_5H_5N) (Found: C, 59·4; H, 5·9; N, 10·7%), were obtained. On storage of the aqueous mother-liquors a small quantity of 1-(2-deoxy-D-galactosyl)benziminazole (*A*) (0·24 g.), m. p. 214°, $[\alpha]_D^{22}$ −16·0° (*c* 1·0 in C_5H_5N), was deposited. A mixture of the isomers melted at 199—205°.

Isomerisation of 1-(*2-Deoxy-D-galactosyl*)*benziminazole* (B).—The glycosylamine (100 mg.) in 0·1N-hydochloric acid (4·4 c.c.) and water (5·6 c.c.) was boiled under reflux. The reaction was followed polarimetrically and was complete in 15 min. The solution was neutralised with sodium hydroxide and concentrated. On cooling, 1-(2-deoxy-D-galactosyl)benziminazole (*A*), m. p. 212—213°, separated. The yield was low and the mother-liquors were brown. As neither benziminazole isomer gave a brown solution when boiled with dilute alkali some hydrolysis was indicated during the acid treatment. 2-Deoxy-D-galactose was shown to give no colour in boiling dilute hydrochloric acid but did yield a brown solution when boiled with dilute alkali.

1-(*Tri*-O-*acetyl*-*2-deoxy*-D-*galactosyl*)*benziminazole Picrate*.—1-(2-Deoxy-D-galactosyl)benziminazole (*A*) (250 mg.) was acetylated with fused sodium acetate (250 mg.) and acetic anhydride (10 c.c.) at 100° for 1 hr. The syrupy product was isolated by standard procedures and was treated with a slight excess of saturated ethanolic picric acid: 1-(*tri*-O-*acetyl*-*2-deoxy*-D-*galactosyl*)*benziminazole picrate* (250 mg.) was obtained as yellow needles, m. p. 158°, $[\alpha]_D^{14}$ ±0° (*c* 1·2 in $CHCl_3$) (Found: C, 48·6; H, 4·1; N, 11·3. $C_{19}H_{22}O_7N_2,C_6H_3O_7N_3$ requires C, 48·4; H, 4·1; N, 11·3%).

1-(*2-Deoxy*-3 : 4(?)-O-iso*propylidene*-D-*galactosyl*)*benziminazole*.—Concentrated sulphuric acid (4·8 c.c.) was added dropwise to a suspension of finely powdered 1-(2-deoxy-D-galactosyl)-benziminazole (*A*) (2·0 g., dried for 3 hr. at 61°/20 mm. over P_2O_5) in dry acetone (120 c.c.) at 0°. After 1 hr. at room temperature the solution was cooled at 0° and added to a stirred solution of anhydrous sodium carbonate (20 g.) in ice-water (80 c.c.). The solution was evaporated at 50° to remove acetone, and the resulting suspension was extracted with chloroform (3 × 100 c.c.). The extracts were washed with water, dried (Na_2SO_4), and evaporated to a solid which was recrystallised from aqueous ethanol. 1-(*2-Deoxy*-3 : 4(?)-O-iso*propylidene*-D-*galactosyl*)*benziminazole* (0·63 g.) was obtained as needles, m. p. 218—219° (decomp.), $[\alpha]_D^{22}$ −11·5° (*c* 3·12 in C_5H_5N) (Found: C, 62·8; H, 6·55; N, 9·3. $C_{16}H_{20}O_4N_2$ requires C, 63·2; H, 6·6; N, 9·2%). When the mother-liquors were allowed to evaporate slowly more needles separated accompanied by some large colourless prisms. The latter were separated and crystallised from aqueous-ethanol. Colourless prisms of the *isomer* (0·16 g.), m. p. 204—205°, $[\alpha]_D^{17}$ −64·7° (*c* 3·09 in C_5H_5N) (Found: C, 62·9; H, 6·6; N, 9·5%), were obtained.

The first *iso*propylidene derivative A (50 mg.) was heated under reflux in water (2·8 c.c.) containing 0·1N-hydrochloric acid (2·2 c.c.). The reaction was complete in 5 min., as indicated polarimetrically. After neutralisation 1-(2-deoxy-D-galactosyl)benziminazole (*A*) (16 mg.), m. p. 214°, was obtained. Similar procedure with the second isomer (75 mg.) also gave compound (*A*).

1-(*2-Deoxy*-D-*glucosyl*)*benziminazole*.—Crude tri-*O*-acetyl-2-deoxy-D-glucosyl bromide (from 20 g. of tri-*O*-acetyl-D-glucal) was added to a suspension of benziminazolylsilver (16·6 g.) in xylene (500 c.c.). After 30 minutes' heating at 120° the mixture was worked up and

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deacetylated according to the procedure developed, and isolated as the picrate. 1-(2-*Deoxy*-D-*glucosyl*)*benziminazole picrate* (5·54 g.) was obtained as orange-yellow needles, m. p. 153—154° (decomp.), $[\alpha]_D^{15}$ −17·3° (*c* 2·08 in C_5H_5N) (Found: C, 45·7; H, 3·9; N, 14·3. $C_{13}H_{16}O_4N_2,C_6H_3O_7N_3$ requires C, 46·25; H, 3·9; N, 14·2%). This picrate (5·2 g.), water (200 c.c.), nitrobenzene (100 c.c.), and concentrated hydrochloric acid (5 c.c.) were shaken together vigorously until the solid had dissolved. The aqueous layer was separated and extracted with nitrobenzene (100 c.c. and 3 × 50 c.c.) and then chloroform (3 × 25 c.c.). After concentration (to 40 c.c.) under reduced pressure the solution was made alkaline (5 c.c. of concentrated ammonia) and rapidly filtered. Solid separated which was collected and recrystallised from ethanol. 1-(2-*Deoxy*-D-*glucosyl*)*benziminazole* was obtained as large prisms, m. p. 196°, $[\alpha]_D^{22}$ −35·2° (*c* 1·19 in C_5H_5N) (Found: C, 59·2; H, 6·1; N, 10·8. $C_{13}H_{16}O_4N_2$ requires C, 59·1; H, 6·1; N, 10·6%).

1-(2 : 6-*Dideoxy*-D-*galactosyl*)*benziminazole*.—Di-*O*-acetyl-D-fucal (m. p. 50—52°, $[\alpha]_D^{25}$ −7·1° in acetone) (2·25 g.) was dissolved in dry benzene (50 c.c.) at 0° and the solution was saturated with dry hydrogen chloride. Evaporation at 40° and re-evaporation with benzene (2 × 50 c.c.) yielded crude di-*O*-acetyl-2 : 6-dideoxy-D-galactosyl chloride as a pale yellow syrup which was added in the minimum of dry xylene to a suspension of benziminazolylsilver (5 g.) in dry xylene (75 c.c.), and the stirred mixture was heated at 110° for 1 hr. After evaporation of the filtrate the residue was washed down an alumina column with chloroform. The washings were evaporated to a pale brown syrup (2·2 g.) which was treated in ethanol (20 c.c.) with a slight excess of saturated ethanolic picric acid. 1-(*Di*-*O*-*acetyl*-2 : 6-*dideoxy*-D-*galactosyl*)*benziminazole picrate* (1·4 g.) was obtained as pale yellow needles, m. p. 168°, $[\alpha]_D^{20}$ +107·8° (*c* 2·54 in C_5H_5N) (Found: C, 48·9; H, 4·0; N, 12·45. $C_{17}H_{20}O_5N_2,C_6H_3O_7N_3$ requires C, 49·2; H, 4·1; N, 12·5%). This compound (1·35 g.) was freed from picric acid by dissolution in the minimum amount of chloroform and by passage through alumina (50 g.; 8 × 3 cm.). The column was washed with more chloroform (200 c.c.). Evaporation yielded a syrup which crystallised on trituration with ethanol. Recrystallisation from ethanol–light petroleum (b. p. 60—80°) afforded 1-(*di*-O-*acetyl*-2 : 6-*dideoxy*-D-*galactosyl*)*benziminazole* (0·45 g.) as prisms, m. p. 206—207°, $[\alpha]_D^{20}$ +201·7° (*c* 2·34 in $CHCl_3$) (Found: C, 61·6; H, 6·0; N, 8·7. $C_{17}H_{20}O_5N_2$ requires C, 61·4; H, 6·1; N, 8·4%). The material (0·40 g.) was deacetylated in dry methanol (50 c.c.) containing sodium methoxide. On recrystallisation from water 1-(2 : 6-*dideoxy*-D-*galactosyl*)-*benziminazole hemihydrate* was obtained as needles, m. p. 185—186°, $[\alpha]_D^{18}$ −52·4° (*c* 2·1 in C_5H_5N) (Found: C, 61·05; H, 6·8; N, 10·9. $C_{13}H_{16}O_3N_2,0{\cdot}5H_2O$ requires C, 60·7; H, 6·7; N, 10·9%). The mother-liquors were adjusted to pH 2 by addition of dilute hydrochloric acid and an excess of saturated aqueous picric acid was added. Recrystallisation from water of the yellow precipitate yielded 1-(2 : 6-*dideoxy*-D-*galactosyl*)*benziminazole picrate* as yellow needles, m. p. 161—162° (decomp.) (Found: C, 48·1; H, 3·8; N, 14·9. $C_{13}H_{16}O_3N_2,C_6H_3O_7N_3$ requires C, 47·8; H, 4·0; N, 14·7%).

1-(2-*Deoxy*-L-*ribosyl*)*benziminazole*.—A solution of di-*O*-acetyl-L-arabinal (5 g.) in dry benzene (35 c.c.) was saturated at room temperature with dry hydrogen chloride. After evaporation at 30° dry benzene (80 c.c.) was distilled over the residue. Crude di-*O*-acetyl-2-deoxy-L-ribosyl chloride in the minimum of dry xylene was added to a suspension of benziminazolylsilver (8·4 g.) in dry xylene. The mixture was heated at 110° for 1 hr. and worked up by the usual procedure to give a brown gum (6·05 g.), a portion (250 mg.) of which afforded a *picrate* as yellow needles (222 mg.) (from ethanol), m. p. 176°, $[\alpha]_D^{17}$ −13·9° (*c* 3·6 in C_5H_5N) (Found: C, 48·3; H, 3·7; N, 12·7. $C_{16}H_{18}O_5N_2,C_6H_3O_7N_3$ requires C, 48·3; H, 3·9; N, 12·8%). Cooley *et al.*[4] give m. p. 167—168°, $[\alpha]_D^{26}$ −8·6° (C_5H_5N), for a compound from 2-deoxy-D-ribose. The main bulk of the gum was deacetylated in dry methanol (150 c.c.) containing a trace of sodium methoxide. To the glassy product excess of picric acid was added and the oily deposit was crystallised and collected (3·25 g.). Recrystallisation from water yielded a yellow solid which was a mixture of the required product and benziminazole picrate. The solid was dissolved in aqueous methanol (100 c.c.) and shaken with Amberlite resin IRA-400(OH) (30 g.) until the yellow colour was discharged. Evaporation of the filtrate gave a colourless gum which crystallised after 3 months. Recrystallisation from water yielded 1-(2-*deoxy*-L-*ribosyl*)*benziminazole* (0·107 g.), m. p. 183°, $[\alpha]_D^{17}$ −33·9° (*c* 1·89 in C_5H_5N) (Found: C, 61·2; H, 6·4; N, 12·35. $C_{13}H_{14}O_3N_2$ requires C, 61·5; H, 6·0; N, 12·0%). This compound gave a Dische diphenylamine test, but much more slowly than 2-deoxy-L-ribose.

1-D-*Galactosyl*-5 : 6-*dimethylbenziminazole*.—A mixture of tetra-*O*-acetyl-α-D-galactosyl

bromide (5·34 g.), 5 : 6-dimethylbenziminazole (4·17 g.), and dry dioxan (15 c.c.) was heated at 100° for 1 hr. Dry benzene (30 c.c.) was added to the cooled mixture and after 2 hr. 5 : 6-dimethylbenziminazole hydrobromide (2·7 g.) was collected and washed with benzene. Removal of solvent from the filtrate and washings gave a brown syrup from which 5 : 6-*dimethyl*-1-(*tetra*-O-*acetyl*-D-*galactosyl*)*benziminazole picrate* was obtained as yellow needles, m. p. 182—184°, $[\alpha]_D^{23}$ +55·8° (*c* 1·18 in $CHCl_3$) (Found: C, 49·2; H, 4·7; N, 10·0. $C_{23}H_{28}O_9N_3,C_6H_3O_7N_3$ requires C, 49·4; H, 4·4; N, 9·9%). This acetate was freed from picric acid by passage in chloroform through alumina (16 × 3 cm.). Evaporation yielded a pale yellow glass (3·6 g.) which was deacetylated (Zemplén). 1-D-*Galactosyl*-5 : 6-*dimethylbenziminazole* (0·84 g.) was obtained, having m. p. 269° (decomp.) (from ethanol), $[\alpha]_D^{17}$ −29·4° (*c* 0·54 in C_5H_5N) (Found: C, 58·6; H, 6·5; N, 9·0. $C_{15}H_{20}O_5N_2$ requires C, 58·45; H, 6·5; N, 9·1%) [*picrate*, orange needles (from ethanol), m. p. 211° (decomp.) (Found: C, 46·55; H, 4·5. $C_{15}H_{20}O_5N_2,C_6H_3O_7N_3$ requires C, 46·9; H, 4·3%)].

1-(2-*Deoxy*-D-*galactosyl*)-5 : 6-*dimethylbenziminazole*.—This compound was prepared as outlined above from crude tri-*O*-acetyl-2-deoxy-D-galactosyl bromide (from 10·25 g. of tri-*O*-acetyl-D-galactal) in dry xylene (200 c.c.) and 5 : 6-dimethylbenziminazolylsilver (10 g.). 5 : 6-*Dimethyl*-1-(*tri*-O-*acetyl*-2-*deoxy*-D-*galactosyl*)*benziminazole picrate* (4·5 g.) was obtained as yellow needles (from ethanol), m. p. 181°, $[\alpha]_D^{23}$ −3·5° (*c* 1·15 in $CHCl_3$) (Found: C, 50·0; H, 4·4; N, 11·1. $C_{21}H_{26}O_7N_2,C_6H_3O_7N_3$ requires C, 50·1; H, 4·5; N, 10·8%). Removal of picric acid from this material (4·0 g.) was effected by passage in chloroform through alumina. Evaporation of the effluent gave a straw-coloured glass (2·1 g.) which was deacetylated (Zemplén) to 1-(2-*deoxy*-D-*galactosyl*)-5 : 6-*dimethylbenziminazole* (1·15 g., 10%), prisms (from aqueous ethanol), m. p. 225°, $[\alpha]_D^{23}$ −32·4° (*c* 1·05 in C_5H_5N) (Found: C, 61·9; H, 6·8; N, 9·7. $C_{15}H_{20}O_4N_2$ requires C, 61·7; H, 6·9; N, 9·6%) {*picrate* (from ethanol), orange needles, m. p. 193° (decomp.) (Found: C, 48·2; H, 4·3; N, 13·4. $C_{15}H_{20}O_4N_2,C_6H_3O_7N_3$ requires C, 48·4; H, 4·45; N, 13·4%)}.

Acid Hydrolysis of 1-*Glycosylbenziminazoles*.—The following compounds were examined: (*a*) 1-β-D-galactosylbenziminazole; (*b*) 1-(2-deoxy-D-galactosyl)benziminazole (*A*); (*c*) 1-(2 : 6-dideoxy-D-galactosyl)benziminazole hemihydrate. A solution of each substance (10 mg.) in 6N-hydrochloric acid (2 c.c.) was heated in a sealed tube for 12 hr. at (i) 100° and (ii) 150°. Some charring occurred in all the tubes except (*a*) (i). The contents of each tube were evaporated to dryness at 30° and in each case an aqueous solution of the gummy residue was examined chromatographically on Whatman No. 1 paper by the ascending technique [19] with an irrigating solvent comprising the organic layer of a butan-1-ol–acetic acid–water (4 : 1 : 5, v/v) mixture for compounds (*a*) and (*b*), and the organic layer of butan-1-ol–water for compound (*c*). The reference compounds were the original glycosylamines (200 μg. per spot) and benziminazole (100 μg. per spot). The hydrolysate spots were neutralised with ammonia before drying. The various substances were located on the developed chromatograms by photography in filtered ultraviolet light.[20] The benziminazole spots were identified by spraying the papers with tetramminocupric sulphate solution, the free base being revealed (after drying) as a red spot on a pale blue background. Ammoniacal solutions of cobaltous chloride or nickel sulphate could be used as spray reagents for the detection of benziminazoles. A violet spot on a brown, and a violet spot on a green, background respectively were obtained but the colour contrasts were inferior to that obtained with tetramminocupric sulphate.

A qualitative estimate of the extent of hydrolysis is shown in the Table.

	Compounds detected on chromatogram of hydrolysate	Hydrolysis	
100°	150°	100°	150°
(*a*) Glycosylamine only	Glycosylamine + benziminazole (faint spot)	Nil	Slight
(*b*) Glycosylamine + benziminazole	Benziminazole only	~50%	Complete
(*c*) Benziminazole only	Benziminazole only	Complete	Complete

In a further experiment, 1-β-D-galactosylbenziminazole (0·0086 g.) was heated in a sealed tube at 100° for 3 days with 6N-hydrochloric acid (5 c.c.). No charring was observed. The solution was neutralised with sodium hydroxide, diluted (to 60 c.c.), and treated with 0·25N-sodium

[19] Williams and Kirby, *Science*, 1948, **107**, 481.
[20] Markham and Smith, *Biochem. J.*, 1949, **45**, 294.

periodate. On the assumption that any D-galactose liberated by hydrolysis would be destroyed in the experimental conditions, the periodate oxidation indicated 97% recovery of the glycosylamine.

Biological Activity of Some Benziminazole Derivatives.—The following compounds were tested for growth inhibition of *E. coli* 15: (i) 1-β-D-galactosylbenziminazole; (ii) 1-(2-deoxy-D-galactosyl)benziminazole (*B*); (iii) 1-(2-deoxy-D-galactosyl)benziminazole (*A*); (iv) 1-(2 : 6-dideoxy-D-galactosyl)-, (v) 1-β-D-galactosyl-5 : 6-dimethyl-, (vi) 1-(2-deoxy-D-galactosyl)-5 : 6-dimethyl-, (vii) 4-trifluoromethyl-,[21] and (viii) 5-trifluoromethyl-benziminazole.[21] The basal nutrient medium was a solution of peptone 1%, " Lemco " 1%, and sodium chloride 0·5%, and a series of 10 tubes were prepared for each compound to be tested. The first tube (T_1) of each series contained the test compound at a concentration of 1 part in 2000 and the dilution was doubled for each successive tube. The growth attained by the organism at a suitable time after inoculation was estimated visually by comparison with controls. Results were as follows:

Benziminazole	Time of growth (hr.)	T_1	T_2	T_3	T_4—T_{10}
4-Trifluoromethyl-	16	—	−+−	±	+
5-Trifluoromethyl-	16	—	−+−	±	+
1-(2-Deoxy-D-galactosyl)-5 : 6-dimethyl-	72	—	−+−	±	+

(+ = Growth equal to control; − = no growth.)

All the other compounds allowed growth equal to that of the control. The first two compounds also showed some activity against *A. aerogenes* when tested in a similar manner.

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[21] Sykes and Tatlow, *J.*, 1952, 4078.

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74. *Some Dichloro- and Dibromo-derivatives of* 1 : 2 : 3 : 4-*Tetrahydrophenazine and* cis-1 : 2 : 3 : 4 : 5 : 10 : 11 : 12-*Octahydrophenazine.**

By RUTH M. SCOTT and MURIEL TOMLINSON.

It has been shown that whereas halogenation of 5-acetyl-1 : 2 : 3 : 4 : 5 : 10 : 11 : 12-octahydrophenazine affords 6 : 8-dichloro- and 6 : 8-dibromo-compounds, 5 : 10-diacetyl-1 : 2 : 3 : 4 : 5 : 10 : 11 : 12-octahydrophenazine is dibrominated in the 7- and the 8-position.

THEORETICAL considerations suggested that the compound $C_{16}H_{18}O_2N_2Br_2$, m. p. 202—204°, obtained[1] by bromination of *cis*-5 : 10-diacetyl-1 : 2 : 3 : 4 : 5 : 10 : 11 : 12-octahydrophenazine (I; R = R′ = Ac; X = H) is most probably *cis*-5 : 10-diacetyl-7 : 8-dibromo-1 : 2 : 3 : 4 : 5 : 10 : 11 : 12-octahydrophenazine (I; R = R′ = Ac; X = Br); whereas the isomeric substance, m. p. 118—120°, obtained by bromination and subsequent acetylation of *cis*-5-acetyl-1 : 2 : 3 : 4 : 5 : 10 : 11 : 12-octahydrophenazine (I; R = Ac; R′ = X = H) is 5 : 10-diacetyl-6 : 8-dibromo-1 : 2 : 3 : 4 : 5 : 10 : 11 : 12-octahydrophenazine† (II; R = R′ = Ac; X = Br). Synthesis of these two diacetyldibromo-octahydrophenazines has now proved that this is so.

Chlorination of the compound (I; R = R′ = Ac; X = H) did not afford crystalline material but when 5-acetyl-1 : 2 : 3 : 4 : 5 : 10 : 11 : 12-octahydrophenazine was chlorinated

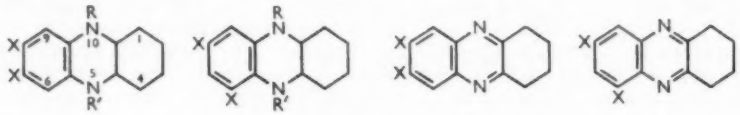
* The compounds described in *J.*, 1956, 794, are 1 : 2 : 3 : 4 : 5 : 10 : 11 : 12-octahydrophenazine and its 9 : 10-derivatives, according to the numbering used in this paper.

† This and all other octahydrophenazines in this paper are presumably *cis*-compounds.

[1] Earle and Tomlinson, *J.*, 1956, 794.

in acetic acid it gave, after acetylation, a substance which has been identified as 5 : 10-diacetyl-6 : 8-dichloro-1 : 2 : 3 : 4 : 5 : 10 : 11 : 12-octahydrophenazine (II; R = R′ = Ac; X = Cl).

These dichloro- and dibromo-phenazines have been synthesised from the appropriate 1 : 2-diamino-dichloro- and -dibromo-benzene and 2-hydroxy*cyclo*hexanone. It was



(I) (II) (III) (IV)

shown[1] that when *o*-phenylenediamine is condensed with 2-hydroxy*cyclo*hexanone, equimolecular quantities of 1 : 2 : 3 : 4-tetrahydro- (III; X = H) and *cis*-1 : 2 : 3 : 4 : 5 : 10 : 11 : 12-octahydro-phenazine (II; R = R′ = X = H), compounds previously described by Clemo and McIlwain,[2,3] are produced. With the dihalogeno-*ortho*-diamines used in this work, in only one instance, namely with 1 : 2-diamino-4 : 5-dichlorobenzene, were both the tetrahydro- (III; X = Cl) and the octahydro-phenazines (I; R = R′ = H; X = Cl) obtained. In all other cases the sole product was the dihalogenotetrahydrophenazine. These chloro- and bromo-tetrahydrophenazines are readily reduced catalytically to 1 : 2 : 3 : 4 : 5 : 10 : 11 : 12-octahydrophenazine but carefully controlled hydrogenation, in the presence of acetic anhydride, affords monoacetyl derivatives of the corresponding dihalogeno-octahydro-compounds, and the monoacetyl compounds obtained in this way from 6 : 8-dichloro- (IV; X = Cl) and 6 : 8-dibromo-1 : 2 : 3 : 4-tetrahydrophenazine (IV; X = Br) were identical with those obtained by chlorination and bromination, respectively, of 5-acetyl-1 : 2 : 3 : 4 : 5 : 10 : 11 : 12-octahydrophenazine. The position of the acetyl group here is not proved, but steric considerations leave little doubt that these compounds are 5-acetyl-6 : 8-dichloro- (II; R = Ac, R′ = H; X = Cl) and 5-acetyl-6 : 8-dibromo-1 : 2 : 3 : 4 : 5 : 10 : 11 : 12-octahydrophenazine (II; R = Ac; R′ = H; X = Br), respectively.

Of the diamines used here, the 3 : 5-dichloro- and 3 : 5-dibromo-compounds were prepared by catalytic reduction of the corresponding 2-nitro-amines; 1 : 2-diamino-4 : 5-dichlorobenzene was prepared from 1 : 2 : 4-trichlorobenzene,[4] while 1 : 2-diamino-4 : 5-dibromobenzene was obtained from 1 : 2-dibromobenzene by dinitration and subsequent reduction.[5]

Experimental

1 : 2-*Diamino*-3 : 5-*dichlorobenzene*.—4 : 6-Dichloro-2-nitroaniline (20 g.) [prepared by chlorinating *o*-nitroaniline in acetic acid (compare Holleman and van Haeften [6])] in tetrahydrofuran (60 c.c.) was hydrogenated over Raney nickel at 5 atm. and room temperature, until the solution became colourless. Dilution with water, after removal of the catalyst, yielded a solid (10 g.) which crystallised from alcohol to give 1 : 2-diamino-3 : 5-dichlorobenzene as needles, m. p. 60—61°. 1 : 2-Diamino-3 : 5-dibromobenzene (12 g.), needles, m. p. 83°, was similarly prepared from the nitro-compound (15 g.).

1 : 2-*Diamino*-4 : 5-*dibromobenzene*.—1 : 2-Dibromo-4 : 5-dinitrobenzene (2 g.) and stannous chloride (11·6 g.) were mixed and added slowly to hydrochloric acid (50 c.c.). The mixture was stirred at 100° until it became colourless, and the solid was collected and decomposed with sodium hydroxide. The precipitated diamine crystallised from alcohol as needles, m. p. 155° (sintering at 140°) (Found: C, 27·5; H, 2·5. Calc. for $C_6H_6N_2Br_2$: C, 27·1; H, 2·3%). Schiff [5] gives m. p. 137°.

[1] Clemo and McIlwain, *J.*, 1934, 1991.
[2] *Idem*, *J.*, 1936, 259.
[4] Acheson, Taylor, and Tomlinson, *J.*, 1958, 3750.
[5] Schiff, *Monatsh.*, 1890, **11**, 338.
[6] Holleman and van Haeften, *Rec. Trav. chim.*, 1921, **40**, 67.

Condensation of 1 : 2-*Diamino*-4 : 5-*dichlorobenzene with* 2-*Hydroxy*cyclo*hexanone*.—1 : 2-Diamino-4 : 5-dichlorobenzene (6 g.) and 2-hydroxy*cyclo*hexanone (4·2 g.) were powdered together and heated at 140° until evolution of water vapour ceased. The mass solidified and was recrystallised from alcohol from which separated 7 : 8-*dichloro*-1 : 2 : 3 : 4-*tetrahydrophenazine* (3·5 g.) as needles, m. p. 183·5° (Found: C, 57·2; H, 4·1. $C_{12}H_{10}N_2Cl_2$ requires C, 56·9; H, 4·0%). Concentration of the mother liquor to half-bulk afforded needles (3 g.), which on further recrystallisation from alcohol gave 7 : 8-*dichloro*-1 : 2 : 3 : 4 : 5 : 10 : 11 : 12-*octahydrophenazine*, m. p. 152° (Found: C, 56·3; H, 5·2. $C_{12}H_{14}N_2Cl_2$ requires C, 56·0; H, 5·5%).

5-*Acetyl*-7 : 8-*dichloro*-1 : 2 : 3 : 4 : 5 : 10 : 11 : 12-*octahydrophenazine*.—A solution of 7 : 8-dichloro-1 : 2 : 3 : 4-tetrahydrophenazine (2·39 g.) in acetic acid (130 c.c.) and acetic anhydride (20 c.c.) was warmed with a little palladium–charcoal and then filtered and hydrogenated over fresh catalyst (0·3 g.; 10% Pd) until hydrogen (466 c.c. at 16·5° and 741 mm.) had been absorbed. Dilution with aqueous potassium acetate precipitated 5-*acetyl*-7 : 8-*dichloro*-1 : 2 : 3 : 4 : 5 : 10 : 11 : 12-*octahydrophenazine* which crystallised from alcohol as needles, m. p. 216° (Found: C, 56·5; H, 5·2. $C_{14}H_{16}ON_2Cl_2$ requires C, 56·2; H, 5·3%).

5 : 10-*Diacetyl*-7 : 8-*dichloro*-1 : 2 : 3 : 4 : 5 : 10 : 11 : 12-*octahydrophenazine*.—This was obtained when the above octahydro-compound or its 9-acetyl derivative was boiled with acetic anhydride (20 min.). It separated from alcohol as needles, m. p. 166—167° (Found: C, 56·0; H, 5·5. $C_{16}H_{18}O_2N_2Cl_2$ requires C, 56·3; H, 5·3%).

7 : 8-*Dibromo*-1 : 2 : 3 : 4-*tetrahydrophenazime*.—Condensation of 1 : 2-diamino-4 : 5-dibromobenzene (10·3 g.) with 2-hydroxy*cyclo*hexanone (4·3 g.) at 110—130° (30 min.) gave a brown mass which crystallised (6·8 g.) on trituration with alcohol. Recrystallisation from light petroleum (b. p. 60—80°) gave 7 : 8-*dibromo*-1 : 2 : 3 : 4-*tetrahydrophenazine* as needles, m. p. 188·5° (Found: C, 42·2; H, 2·9. $C_{12}H_{10}N_2Br_2$ requires C, 42·1; H, 2·9%). Attempts to isolate the octahydro-compound or an acetyl derivative of it from the mother liquor were unsuccessful.

5-*Acetyl*-7 : 8-*dibromo*-1 : 2 : 3 : 4 : 5 : 10 : 11 : 12-*octahydrophenazine*.—This was prepared by reductive acetylation (as above) of the tetrahydro-compound (0·83 g.). Hydrogen (115 c.c. at 18·5° and 754 mm.) was absorbed, and addition of aqueous ammonia precipitated 5-*acetyl*-7 : 8-*dibromo*-1 : 2 : 3 : 4 : 5 : 10 : 11 : 12-*octahydrophenazine* which crystallised as prisms, m. p. 190—192° (Found: C, 43·7; H, 4·2. $C_{14}H_{16}ON_2Br_2$ requires C, 43·3; H, 4·1%).

5 : 10-*Diacetyl*-7 : 8-*dibromo*-1 : 2 : 3 : 4 : 5 : 10 : 11 : 12-*octahydrophenazine*.—When the solution from the above hydrogenation was boiled for 20 min. and then neutralised with aqueous ammonia, 5 : 10-diacetyl-7 : 8-dibromo-1 : 2 : 3 : 4 : 5 : 10 : 11 : 12-octahydrophenazine was obtained, m. p. 202—204° (from alcohol) not depressed by admixture with the compound, m. p. 202—204°, obtained by bromination of 5 : 10-diacetyl-1 : 2 : 3 : 4 : 5 : 10 : 11 : 12-octahydrophenazine.

6 : 8-*Dichloro*-1 : 2 : 3 : 4-*tetrahydrophenazine*.—1 : 2-Diamino-3 : 5-dichlorobenzene (1·7 g.) and 2-hydroxy*cyclo*hexanone (1·13 g.) were condensed at 120°. The product crystallised in contact with alcohol and was recrystallised from alcohol giving 6 : 8-*dichloro*-1 : 2 : 3 : 4-*tetrahydrophenazine*, m. p. 116—116·5° (Found: C, 56·7; H, 3·9. $C_{12}H_{10}N_2Cl_2$ requires C, 56·9; H, 3·9%). No octahydro-compound could be isolated.

5-*Acetyl*-6 : 8-*dichloro*-1 : 2 : 3 : 4 : 5 : 10 : 11 : 12-*octahydrophenazine*.—(*a*) On reductive acetylation (as above) 6 : 8-dichloro-1 : 2 : 3 : 4-tetrahydrophenazine (1·1 g.) absorbed hydrogen (206 c.c. at 14° and 755 mm.) giving 5-*acetyl*-6 : 8-*dichloro*-1 : 2 : 3 : 4 : 5 : 10 : 11 : 12-*octahydrophenazine*, plates, m. p. 132—133° (from alcohol).

(*b*) A solution of chlorine (3·7 g.) in acetic acid was added to 5-acetyl-1:2:3:4:5:10:11:12-octahydrophenazine (6 g.) also in acetic acid. The mixture was immediately diluted with water, and the gummy precipitate was redissolved in acetic acid and precipitated again. It then crystallised from alcohol as plates, m. p. 130—132° (3·3 g.), identical (mixed m. p.) with the above substance (Found: C, 56·8; H, 5·4; N, 9·5. $C_{14}H_{14}ON_2Cl_2$ requires C, 56·2; H, 5·4; N, 9·4%). When this was boiled with acetic anhydride and a trace of sulphuric acid it gave 5 : 10-*diacetyl*-6 : 8-*dichloro*-1 : 2 : 3 : 4 : 5 : 10 : 11 : 12-*octahydrophenazine*, plates (from alcohol), m. p. 132·5—133·5° depressed by admixture with the above (Found: C, 56·2; H, 5·3; N, 8·1. $C_{16}H_{18}O_2N_2Cl_2$ requires C, 56·3; H, 5·3; N, 8·2%).

6 : 8-*Dibromo*-1 : 2 : 3 : 4-*tetrahydrophenazine*.—1 : 2-Diamino-3 : 5-dibromobenzene (30 g.) and 2-hydroxy*cyclo*hexanone (12·4 g.) condensed at 110—130° (20 min.) gave 6 : 8-*dibromo*-1 : 2 : 3 : 4-*tetrahydrophenazine* (17·9 g.), needles, m. p. 105° (from alcohol) (Found: C, 42·3;

H, 3·1; N, 8·0. $C_{12}H_{10}N_2Br_2$ requires C, 42·1; H, 2·9; N, 8·2%): on reductive acetylation this tetrahydro-compound (2·47 g.) in acetic acid (150 c.c.) and acetic anhydride (20 c.c.) absorbed hydrogen (370 c.c. at 14° and 748 mm.) to give 5-acetyl-6 : 8-dibromo-1 : 2 : 3 : 4 : 5 : 10 : 11 : 12-octahydrophenazine, m. p. 117—118°; the m. p. was slightly raised on admixture with the compound, m. p. 118—119°, prepared by bromination of 9-acetyl-octahydrophenazine. 5 : 10-Diacetyl-6 : 8-dibromo-1 : 2 : 3 : 4 : 5 : 10 : 11 : 12-octahydrophenazine was obtained from this by further acetylation, and its m. p. 164·5° was not depressed by admixture with the diacetyl compound, m. p. 164—165°, prepared by brominating and acetylating 5-acetyl-1 : 2 : 3 : 4 : 5 : 10 : 11 : 12-octahydrophenazine.

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75. *Oxidation of Polyhalogeno-compounds. Part III.*[1] *Thermal Oxidation of Some Chlorofluoroethanes.**

By R. N. HASZELDINE and F. NYMAN.

Thermal oxidation with molecular oxygen of the compounds $CF_3{\cdot}CHCl_2$ and $CF_3{\cdot}CH_2Cl$ in presence of chlorine as initiator gives trifluoroacetic acid in high yield. The compound $CF_3{\cdot}CCl_3$ is more stable and its oxidation is accompanied by complete carbon–carbon bond fission.

PHOTOCHEMICAL oxidation of the chlorofluoroethane $CF_3{\cdot}CCl_3$, $CF_3{\cdot}CHCl_2$, or $CF_3{\cdot}CH_2Cl$ gives high yields of trifluoroacetic acid or trifluoroacetyl chloride.[1] A free-radical reaction scheme was proposed in which the primary step is either photochemical homolysis of a carbon–halogen bond or abstraction of a hydrogen atom by one of chlorine. The thermal oxidation of these compounds, alone or in the presence of chlorine, has now been studied, since if the primary steps are the same as in the photochemical reactions it should be possible to achieve controlled oxidation to trifluoroacetic acid or its precursors. Thermal oxidation would be more convenient than photochemical oxidation for large-scale preparation of trifluoroacetic acid. The results obtained show that 1-chloro-2 : 2 : 2-trifluoroethane and 1 : 1-dichloro-2 : 2 : 2-trifluoroethane give good yields of trifluoroacetic acid. Typical results are summarised in the annexed Table.

The thermal stability of trifluoroacetic acid and trifluoroacetyl chloride in the presence of oxygen, with or without chlorine as sensitiser, was investigated to determine the temperature limitations of a successful thermal oxidation. Trifluoroacetic acid was stable in the presence of oxygen at 200° for up to 24 hr., but at 250° it begins to afford carbon dioxide by oxidation and silicon tetrafluoride by attack on the glass reaction vessel. The addition of chlorine did not decrease the thermal stability of the acid at 200°. The absence of chlorotrifluoromethane from the product showed that chlorinolysis of the acid or decomposition *via* trifluoroacetyl hypochlorite was not occurring; chlorotrifluoromethane is stable under the conditions used.

$$CF_3{\cdot}CO_2H \xrightarrow{Cl_2} CF_3Cl + CO_2 + HCl$$

$$CF_3{\cdot}CO_2H \xrightarrow{Cl_2} HCl + CF_3{\cdot}CO_2Cl \longrightarrow CF_3Cl + CO_2$$

Trifluoroacetyl chloride in the presence of oxygen at 200° was only slightly oxidised during 24 hr.; at 250° slow breakdown to carbon dioxide and silicon tetrafluoride was apparent, but trifluoroacetyl chloride was more stable than trifluoroacetic acid at this temperature.

1 : 1 : 1-Trichlorotrifluoroethane did not react with oxygen below 350°, and at 400°

* Presented at Amer. Chem. Soc. Meeting, New York, 1957. Preliminary communication, *Proc. Chem. Soc.*, 1957, 146.

[1] Part II, *J.*, 1959, 387.

was slowly oxidised to carbon dioxide. The addition of chlorine did not lower the initiation temperature or alter the rate of oxidation. Trifluoroacetyl chloride, if formed, would itself be completely oxidised at 400° under the conditions used, and hence it cannot be deduced directly that the thermal oxidation follows the same path as that proposed earlier for the photochemical oxidation of this ethane. However, the results obtained with the other chlorofluoroethanes suggest that trifluoroacetyl chloride is again the intermediate.

Thermal oxidation of $CF_3 \cdot CO_2H$, $CF_3 \cdot COCl$, $CF_3 \cdot CCl_3$, $CF_3 \cdot CHCl_2$, *and* $CF_3 \cdot CH_2Cl$.

Compound oxidised	Mmoles cpd. taken	Mole ratio O_2 : Cpd.	Mole ratio Cl_2 : Cpd.	Pressure (atm.)	Temp. (c)	Reaction time (hr.)	Oxidation (%)	$CF_3 \cdot CO_2H$ yield or recovery [a] Mmole	%
$CF_3 \cdot CO_2H$	4·76	1·0	—	2·1	200	24	9	4·35	91
$CF_3 \cdot CO_2H$	4·27	1·0	0·7	2·3	200	24	9 [c]	3·88	91
$CF_3 \cdot CO_2H$	3·97	1·0	—	1·7	250	23	100	0	0
$CF_3 \cdot CO_2H$	4·20	1·1	—	2·1	250	8	35	2·72	65
$CF_3 \cdot COCl$	3·88	1·2	—	1·6	200	24	7	3·62 ($CF_3 \cdot COCl$)	93
CFC·OCl	6·01	1·7	—	3·4	250	24	53	2·85 ($CF_3 \cdot COCl$)	47
$CF_3 \cdot CCl_3$	2·52	1·8	—	2·5	400	43	39 [b]	0	0
$CF_3 \cdot CCl_3$	2·94	1·4	2·4	4·2	400	48	44 [a, b]	0	0
$CF_3 \cdot CH_2Cl$	4·35	1·1	—	1·9	200	24	0	0	0
$CF_3 \cdot CH_2Cl$	4·35	1·1	—	1·9	250	23	42 [a, b]	0	0
$CF_3 \cdot CH_2Cl$	4·25	1·1	1·1	2·9	250	23	100 [c]	0·66	16 [d]
$CF_3 \cdot CH_2Cl$	6·15	1·0	1·0	3·6	200	23	93 [c]	1·76	31 [d]
$CF_3 \cdot CH_2Cl$	4·25	1·1	0·2	1·9	200	12	25 [c]	0·77	72 [e]
$CF_3 \cdot CHCl_2$	4·76	1·0	0·1	2·1	200	23	22 [c]	0·97	93 [e]

[a] CO_2 and SiF_4 produced in every experiment.
[b] Products shaken with mercury to remove chlorine before distillation. [c] Thin film of unidentified white solid on wall of tube. [d] $CF_3 \cdot CCl_3$ (1·63 mmole) formed in 38% yield; HCl produced. [e] $CF_3 \cdot CHCl_2$ (0·88 mmole) formed in 15% yield; $CF_3 \cdot CCl_3$ (1·76 mmole) in 31% yield; HCl produced.
[f] HCl also produced.

1-Chloro-2 : 2 : 2-trifluoroethane and oxygen did not react at 200°, and at 250° slowly gave carbon dioxide and silicon tetrafluoride. The rate of oxidation of this ethane at 250° is slower than that of trifluoroacetic acid, so that the absence of the acid from the products is not surprising. When 1-chloro-2 : 2 : 2-trifluoroethane was oxidised in the presence of an equimolar amount of chlorine, reaction took place at a lower temperature, 200°, and a 31% yield of trifluoroacetic acid was obtained. The low yield of acid was primarily due to the concurrent thermal chlorination of the ethane to give 1 : 1-dichloro-2 : 2 : 2-trifluoroethane and 1 : 1 : 1-trichlorotrifluoroethane. Reduction of the amount of chlorine eliminated the unwanted chlorination, and the yield of trifluoroacetic acid increased to 72%. The lower yield (16%) of trifluoroacetic acid accompanying complete oxidation at 250° in the presence of chlorine is clearly caused by the breakdown of the acid. The action of chlorine as sensitiser is clearly to abstract hydrogen to produce the $CF_3 \cdot CHCl$ radical, which is then rapidly oxidised as outlined in Part II.

$$CF_3 \cdot CH_2Cl + Cl \cdot \longrightarrow CF_3 \cdot CHCl \cdot + HCl$$

$$CF_3 \cdot CHCl \cdot \xrightarrow{O_2} CF_3 \cdot COCl, \text{ etc.}$$

The oxidation of 1 : 1-dichloro-2 : 2 : 2-trifluoroethane at 200° in the presence of a small amount of chlorine was even more successful and gave a 93% yield of trifluoroacetic acid. This yield is comparable with the 90% from photochemical oxidation in the presence of chlorine.[1] The chlorine again initiates reaction by hydrogen abstraction to give the $CF_3 \cdot CCl_2 \cdot$ radical, shown earlier to be readily oxidised to trifluoroacetyl chloride.

The main difference between the thermal and the photochemical oxidation of 1-chloro- and 1 : 1-dichloro-2 : 2 : 2-trifluoroethane is that the thermal reaction, even in presence of chlorine as initiator, gives only trifluoroacetic acid and not trifluoroacetyl chloride, whereas the photochemical reaction gives mainly the acyl chloride. A further difference is the importance of using small amounts of chlorine as initiator in the thermal reaction if chlorination to 1 : 1 : 1-trichlorotrifluoroethane, not observed in the photochemical experiments, is to be avoided; the rates of thermal chlorination and oxidation are presumably very similar.

Thermal oxidation of the chlorofluoroethanes, which in other respects are extremely stable chemically, can thus be achieved in simple apparatus and adapted to large-scale production of trifluoroacetic acid with a yield which, though already high, could clearly be enhanced by detailed study of the reactant ratios, temperature, pressure, initiator concentration, use of flow system, etc. The results also reveal that controlled thermal oxidation is a powerful method for the conversion of stable fluorine compounds into useful compounds containing functional groups.

Experimental

General Techniques.—The oxidations were carried out in sealed, 200-ml. Pyrex tubes, filled by condensation from an apparatus for manipulation of volatile compounds *in vacuo*. Oxygen was condensed into the reaction tube from a reservoir attached to the vacuum-system. All reactants were distilled before use and were analytically and spectroscopically pure. The volatile reaction products were transferred to the vacuum-system for distillation and were analysed and identified by b. p., molecular weight, vapour pressure, infrared spectroscopy, etc. Trifluoroacetic acid was often converted into its silver salt for analysis. Yields are based on material consumed. Relevant results, summarised in the Table, are from typical experiments.

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University Chemical Laboratory, Cambridge. [*Received, September 18th,* 1958.]

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76. *Organic Compounds of Zirconium. Part VI.* Reactions of Zirconium Tetrachloride and* iso*Propoxide with Fatty Acids.*

By R. N. Kapoor and R. C. Mehrotra.

Fatty acids with zirconium tetrachloride give tetracarboxylates directly. With zirconium *iso*propoxide only oxygen-bridged compounds of the type $(R{\cdot}CO_2)_3Zr{\cdot}O{\cdot}Zr(CO_2R)_3$ are obtained. By studying the latter reaction stepwise, we find that it is straightforward to the dicarboxylate stage, after which side reactions occur. A mechanism is suggested.

Although there is much recent work on organic derivatives of zirconium, the only reference to its compounds with monocarboxylic acids is that of Ryan and Plechner [1] who claimed the preparation of zirconium tetra-soaps by the reaction:

$$ZrCl_4 + 4R{\cdot}CO_2H + 2CaCO_3 \longrightarrow Zr(R{\cdot}CO_2)_4 + 2CaCl_2 + 2CO_2 + 2H_2O. \quad . \; . \; . \quad (I)$$

On attempting this reaction, we obtained highly hydrolysed derivatives owing to the water produced. Aqueous precipitation methods, even under modified conditions, always yielded hydrolysed products of indefinite composition; zirconium salts, even of strong mineral acids, are readily hydrolysed.

We therefore attempted to prepare zirconium carboxylates in a non-aqueous medium

* Part V, Kapoor and Mehrotra, *J. Amer. Chem. Soc.*, 1958, **80**, 3569.

[1] Ryan and Plechner, *Ind. Eng. Chem.*, 1934, **26**, 909.

from zirconium tetra*iso*propoxide, which is easily obtainable pure and dissolves freely in benzene.

Zirconium *iso*propoxide and excess of a fatty acid (stearic, palmitic, lauric, and caproic) yield [2] basic tricarboxylates $(R{\cdot}CO_2)_3Zr{\cdot}O{\cdot}Zr(CO_2R)_3$ which are unchanged on repeated crystallisation from dioxan. The reaction was carried out in refluxing benzene under a column so that the *iso*propyl alcohol produced could be removed azeotropically with benzene. The alcohol in the azeotrope was estimated. Even when the ratio zirconium *iso*propoxide : fatty acid was more than 1 : 4, not more than 4·5 moles of alcohol per mole of the crystalline *iso*propoxide $Zr(OPr^i)_4,Pr^iOH$ distilled azeotropically. It thus appeared that the replacement of the fifth alcoholic group might be slow owing to steric hindrance, or that a side reaction occurred owing to which a portion of the replaceable alcohol in the alkoxide could not be distilled. For example, the fact that 4·5 mol. of alcohol are replaced can be explained simply if the main reaction is represented by:

$$2Zr(OPr^i)_4,Pr^iOH + 6R{\cdot}CO_2H \longrightarrow 2Zr(OPr^i)(R{\cdot}CO_2)_3 + 8Pr^iOH \quad \text{(ii)}$$

$$Zr(OPr^i)(R{\cdot}CO_2)_3 + R{\cdot}CO_2H \longrightarrow Zr(R{\cdot}CO_2)_4 + Pr^iOH \text{ (slow)} \quad \text{(iii)}$$

$$Zr(OPr^i)(R{\cdot}CO_2)_3 + Zr(R{\cdot}CO_2)_4 \longrightarrow (R{\cdot}CO_2)_3Zr{\cdot}O{\cdot}Zr(CO_2R)_3 + R{\cdot}CO_2Pr^i \quad \text{(iv)}$$

The reaction of zirconium tetra*iso*propoxide with palmitic and stearic acids was carried out stepwise:

$$Zr(OPr^i)_4,Pr^iOH + R{\cdot}CO_2H \longrightarrow Zr(R{\cdot}CO_2)(OPr^i)_3 + 2Pr^iOH \quad \text{(v)}$$

$$Zr(OPr^i)_4,Pr^iOH + 2R{\cdot}CO_2H \longrightarrow Zr(R{\cdot}CO_2)_2(OPr^i)_2 + 3Pr^iOH \quad \text{(vi)}$$

These replacements were rapid and the benzene–*iso*propyl alcohol azeotrope distilled quickly. Tri*iso*propoxyzirconium monostearate and monopalmitate and di*iso*propoxyzirconium distearate and dipalmitate were isolated pure. They are stable to heat under reduced pressure, but are susceptible to atmospheric moisture.

The di-soaps were treated with fatty acids (palmitic or stearic) in the molar ratio 1 : 1. On fractionation almost 1 mol. of alcohol distilled azeotropically, indicating the simple reaction:

$$Zr(OPr^i)_2(R{\cdot}CO_2)_2 + R{\cdot}CO_2H \longrightarrow Zr(OPr^i)(R{\cdot}CO_2)_3 + Pr^iOH \quad \text{(vii)}$$

From the remaining solution, benzene was distilled off under reduced pressure and the solid products were analysed. The zirconium content corresponded to the mono*iso*propoxy-tricarboxylate, but the *iso*propoxy-content was considerably below theoretical. Further the *iso*proxy-content depended on the amount of heating to which the products were subjected. If the mono*iso*propoxytristearate decomposes:

$$Zr(OPr^i)(R{\cdot}CO_2)_3 = O{:}Zr(R{\cdot}CO_2)_2 + R{\cdot}CO_2Pr^i \quad \text{(viii)}$$

the analytical results could be explained. The product from reaction (vii) was treated with dry dioxan; the crystallised zirconium soap on analysis corresponded to a mixture of $ZrO(R{\cdot}CO_2)_2$ and $Zr(OPr^i)(R{\cdot}CO_2)_3$. The sweet-smelling dioxan-soluble portion was a mixture of the fatty acid and ester; on analysis a sample conformed with the decomposition (viii).

The isolation of the *iso*propoxyzirconium tristearate is, therefore, only possible by carrying out the reaction at a low temperature:

$$Zr(OPr^i)_4 + 3R{\cdot}CO_2H \longrightarrow Zr(OPr^i)(R{\cdot}CO_2)_3 + 3Pr^iOH \quad \text{(ix)}$$

The correctness of the overall reaction mechanism (iv) has been further demonstrated by refluxing an equimolecular mixture of the *iso*propoxyzirconium tristearate and the tetrastearate, whereupon the reaction (x) takes place:

$$Zr(OPr^i)(\text{stearate})_3 + Zr(\text{stearate})_4 \longrightarrow O\begin{matrix}Zr(\text{stearate})_3\\ Zr(\text{stearate})_3\end{matrix} + Pr^i(\text{stearate}) \quad \text{(x)}$$

[2] Kapoor and Mehrotra, *Chem. and Ind.*, 1958, 68.

Having failed to prepare zirconium tetra-soaps by the above reaction, we tried to make zirconium tetrachloride react with fatty acids (stearic, palmitic, and myristic). Although the tetrachloride is not appreciably soluble in benzene, it slowly reacted with fatty acids when refluxed and hydrogen chloride was freely evolved. Refluxing was continued until this evolution became negligible, and the solution gave colourless crystals of tetra-soaps:

$$ZrCl_4 + 4R{\cdot}CO_2H \longrightarrow Zr(R{\cdot}CO_2)_4 + 4HCl \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (xi)$$

Repeated crystallisation from benzene did not noticeably change the analysis of the product whose identity is thus confirmed.

Titanium compounds behave similarly.[3]

Experimental

Apparatus.—All-glass apparatus with interchangeable joints was used with care to exclude moisture. All fractionations were carried out in a 60 cm. column packed with Raschig rings and fitted with a total-condensation variable take-off stillhead.

Materials.—Zirconium *iso*propoxide (used as the *iso*propyl alcoholate), prepared by Bradley, Mehrotra, and Wardlaw's method, was repeatedly crystallised from *iso*propyl alcohol [Found: Zr, 23·60; Pr^iO, 76·9. Calc. for $Zr(OPr^i)_4.Pr^iOH$: Zr, 23·53; Pr^iO, 76·21%]. Zirconium tetrachloride (Merck, resublimed G.R. sample) was a fine, pale yellow powder. The fatty acids (decanoic, lauric, myristic, palmitic, and stearic) were Reagent Grade products of B.D.H. or Kahlbaum. They were repeatedly crystallised, then fractionated under reduced pressure.

Benzene ("AnalaR") was dried by storage and fractionation over sodium. Dioxan (B.D.H., Technical) was refluxed with sodium to remove peroxide and then fractionated.

Analyses.—Zirconium was estimated as oxide by direct ignition. The alcohol content of the benzene–alcohol azeotrope was determined by an oxidimetric method [5] which could be applied directly as benzene did not reduce potassium dichromate at room temperature.

Reaction between Zirconium iso*Propoxide and Excess of Fatty Acids.—Procedure.* The methods of preparation being similar, details are given of one preparation only.

Zirconium iso*propoxide and excess of palmitic acid.* Benzene (80 g.) was added to zirconium tetra*iso*propoxide (2·59 g.) and palmitic acid (9·6 g.). The mixture was refluxed under a column (bath temp., 120—130°). About 20 c.c. of the distillate, collected at 71—75° during ½ hr., contained 1 g. of *iso*propyl alcohol. The temperature of the distilling liquid rose at this stage and after about 1 hr. became almost steady at 76°. Nearly 20 c.c. of the distillate, collected at 76—80° during about 2 hr., contained 0·6 g. of the alcohol. The temperature of the distilling liquid eventually became constant at 80° and benzene was collected under a reflux-ratio of 1 : 20. The residue was a colourless mobile solution in benzene, from which a white solid was obtained after removal of the benzene at 40° (bath)/2 mm.

The total *iso*propyl alcohol in the azeotrope was 1·6 g. (Calc. for 4 mol.: 1·9 g.). The product was refluxed with dry dioxan (50 c.c.) for nearly 5 min. at 120° (bath), giving a clear solution which, on cooling, gave white crystals which were washed with dry dioxan and dried [60° (bath)/2 mm.] for 2 hr. [Found: Zr, 10·52%. Calc. for $(C_{15}H_{31}{\cdot}CO_2)Zr{\cdot}O{\cdot}Zr(CO_2C_{15}H_{31})$: Zr, 10·45%].

The dioxan filtrate contained 2·48 g. of free fatty acid and 1·0 g. of *iso*propyl palmitate which were respectively estimated by direct titration with alkali and after hydrolysis in boiling alkali. The quantities expected are 2·5 g. and 1·02 g. if the reaction was:

$$2Zr(OPr^i) + 7R{\cdot}CO_2H \longrightarrow (R{\cdot}CO_2)_3Zr{\cdot}O{\cdot}Zr(CO_2R)_3 + R{\cdot}CO_2Pr^i + 7Pr^iOH$$

Zirconium iso*propoxide and excess of stearic acid.* Zirconium *iso*propoxide (1·34 g.) in benzene (80 g.) and stearic acid (4·42 g.) were treated as above [Found: Zr, 9·71. Calc. for $(C_{17}H_{35}{\cdot}CO_2)_2Zr{\cdot}O{\cdot}Zr(CO_2C_{17}H_{35})_2$: Zr, 9·61%]. Total *iso*propyl alcohol found in the azeotrope was 0·93 g. against 1·03 g. required for 5 mol.

[3] Pande and Mehrotra, *Z. anorg. Chem.*, 1957, **290**, 87, 95; 1957, **291**, 87; *J. prakt. Chem.*, 1957, **5**, 101.

[4] Bradley, Mehrotra, and Wardlaw, *J.*, 1952, 2027.

[5] Mehrotra, *J. Indian Chem. Soc.*, 1953, **30**, 588.

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Zirconium iso*propoxide and excess of lauric acid.* Zirconium *iso*propoxide (1·29 g.) and lauric acid (3·02 g.) in benzene (58 g.) gave a distillate (about 25 g.) between 72—80°. The remaining benzene solution was treated as above, yielding a gum which did not crystallise from dioxan. The gum was heated at 200° (bath)/0·5 mm. for 1 hr. Repetition of the treatment with dioxan, gave a white product [Found: Zr, 12·78. Calc. for $(C_{11}H_{23}\cdot CO_2)_3Zr\cdot O\cdot Zr(CO_2C_{11}H_{23})_3$: Zr, 13·06%].

Zirconium iso*propoxide and excess of decanoic acid.* Zirconium *iso*propoxide (2·13 g.) and decanoic acid (4·16 g.) were allowed to react in benzene (60 g.) as above. The product (a yellow viscous liquid) was treated as for lauric acid [Found: Zr, 13·96%. Calc. for $(C_9H_{19}\cdot CO_2)_3Zr\cdot O\cdot Zr(O_2C\cdot C_9H_{19})_3$: Zr, 14·84%.

Reaction between Zirconium iso*Propoxide and Fatty Acids in Different Molar Ratios.—Tri*iso*propoxyzirconium monostearate.* Benzene (56 g.) was refluxed (bath, 130°) with zirconium *iso*propoxide (1·80 g.) and stearic acid (1·17 g. (molar ratio 1 : 1). The benzene–*iso*propyl alcohol azeotrope collected in 1 hr. contained 0·49 g. of alcohol (Calc., 0·49 g.). A paste was obtained [Found: Zr, 16·49; OPr^i, 32·0. Calc. for $Zr(OPr^i)_2(C_{17}H_{35}\cdot CO_2)$: Zr, 16·52: OPr^i, 32·15%].

*Tri*iso*propoxyzirconium monopalmitate.* Refluxing of zirconium *iso*propoxide (1·41 g.) and palmitic acid (0·93 g.) (molar ratio 1 : 1) in benzene (60 g.) as above gave 0·42 g. of *iso*propyl alcohol in the azeotrope, and a residue [Found: Zr, 17·21; OPr^i, 33·8. Calc. for $Zr(OPr^i)_3(C_{15}H_{31}\cdot CO_2)$: Zr, 17·41; OPr^i, 33·82%].

*Di*iso*propoxyzirconium distearate.* Zirconium *iso*propoxide (2·19 g.) and stearic acid (3·21 g.) (molar ratio 1 : 2) were refluxed (bath, 140°) in benzene (55 g.). The azeotrope, fractionated and collected within 1 hr., contained 1·0 g. of *iso*propyl alcohol (Calc., 1·02 g.) [Found in residue: Zr, 11·28; OPr^i, 15·0. Calc. for $Zr(OPr^i)_2(C_{17}H_{35}\cdot CO_2)_2$: Zr, 11·75; OPr^i, 15·21%].

*Di*iso*propoxyzirconium dipalmitate.* Zirconium *iso*propoxide (2·03 g.) and palmitic acid (2·68 g.) (molar ratio 1 : 2) in benzene as above gave an azeotrope containing 0·940 g. of *iso*-propyl alcohol (Calc., 0·944 g.) and a viscous mass (3·88 g.) which became semi-solid on long storage [Found: Zr, 12·63; OPr^i, 16·30. Calc. for $Zr(OPr^i)_2(C_{15}H_{31}\cdot CO_2)_2$: Zr, 12·66; OPr^i, 16·38%].

Zirconium iso*propoxide and stearic acid (molar ratio* 1 : 3). Zirconium *iso*propoxide (2·05 g.) and stearic acid (4·53 g.) in benzene (65 g.) gave on refluxing under the column a distillate (*ca.* 25 c.c.) at 72—80° containing 1·25 g. of *iso*propyl alcohol (Calc., 1·27 g.). The remaining solution in benzene, treated as above, gave a white product [Found: Zr, 9·10; OPr^i, 1·0. Calc. for $Zr(OPr^i)(C_{17}H_{35}\cdot CO_2)_3$: Zr, 9·10; OPr^i, 5·9%] which when refluxed with dry dioxan (20 c.c.) (bath, 120°) for 10 min. gave a white mass (Found: Zr, 12·40; OPr^i, negligible).

Zirconium iso*propoxide and palmitic acid (molar ratio* 1 : 3). Zirconium *iso*propoxide (2·27 g.) and palmitic acid (4·52 g.) in refluxing benzene (60 c.c.) gave a distillate (*ca.* 25 c.c.) at 72—80° containing 1·37 g. of *iso*propyl alcohol (Calc., 1·40 g. for the replacement of 4 mol.) and a residue [Found: Zr, 9·97; OPr^i, 1·8. Calc. for $Zr(OPr^i)(C_{15}H_{31}\cdot CO_2)_3$: Zr, 9·95; OPr^i, 6·6%] which was treated with dioxan (Found: Zr, 12·87; OPr^i, 1·6%).

*Di*iso*propoxyzirconium dipalmitate and palmitic acid* (1 *mol.*). Palmitic acid (0·76 g.) was refluxed with di*iso*propoxyzirconium dipalmitate (2·16 g.) in benzene (50 c.c. (bath, 130°). The azeotrope, collected in 1 hr., contained 0·17 g. of *iso*propyl alcohol (Calc. 0·18 g.). Removal of excess of benzene under reduced pressure left a low-melting solid (Found: Zr, 10·12; OPr^i, 1·76%) which was treated with dioxan (Found: Zr, 12·76%).

*Mono*iso*propoxyzirconium Tristearate.*—Zirconium tetra*iso*propoxide (2·87 g.; 3 mol.) was added to stearic acid (7·48 g.; 1 mol.) in benzene (60 c.c.). The volatile fractions were removed [30° (bath)/2 mm.] in 3 hr. to leave a residue [Found: Zr, 9·19; OPr^i, 5·7. Calc. for $Zr(OPr^i)(C_{17}H_{35}\cdot CO_2)_3$: Zr, 9·12; OPr^i, 5·9%] which, after refluxing with dry benzene (30 c.c.) for ½ hr. at 110°, removal of volatile fractions (2 mm.) for 2 hr., and refluxing with dry dioxan (20 c.c.), gave crystals (Found: Zr, 12·40; OPr^i, 0·6%).

*Reaction of Mono*iso*propoxyzirconium Tristearate with Zirconium Tetrastearate in Dry Dioxan.*—Dioxan (30 c.c.) was heated (bath, 120°) with mono*iso*propoxyzirconium tristearate (0·94 g.) and zirconium tetrastearate (1·14 g.) (molar ratio of 1 : 1). Cooling of the clear solution gave a white mass {Found: Zr, 9·61. Calc. for $O[Zr(C_{17}H_{35}\cdot CO_2)_3]_2$: Zr, 9·61%} which did not recrystallise from benzene.

Zirconium Tetra-soaps.—Zirconium tetrapalmitate. Palmitic acid (9·54 g.; 4·5 mol.) and the suspension of zirconium tetrachloride (1·92 g.; 1 mol.) in benzene (44 g.) were refluxed for 14 hr. (bath, 100°) until evolution of hydrogen chloride almost ceased and a clear solution was obtained. On storage overnight, a white mass separated. This was recrystallised from

benzene (25 c.c.), filtered off, washed, and dried (40°/2 mm.) for 2 hr. [Found: Zr, 8·13. Calc. for $Zr(C_{15}H_{31}\cdot CO_2)_4$: Zr, 8·19%].

Zirconium tetrapalmitate (*ca.* 2 g.) was refluxed with dry dioxan (20 c.c.) for about 10 min. (bath, 120°). Cooling of the clear solution gave white crystals which were filtered off, washed with dry dioxan, and dried (50°/4 mm.) for 2 hr. (yield 1·8 g.) [Found: Zr, 8·29. Calc. for $Zr(C_{15}H_{31}\cdot CO_2)_4$: Zr, 8·19%].

Zirconium tetrastearate. Zirconium tetrachloride (1·31 g.), benzene (52 g.), and stearic acid (7·98 g.) were treated as above. A portion of the crystalline product [Found: Zr, 7·43. Calc. for $Zr(C_{17}H_{35}\cdot CO_2)_4$: Zr, 7·44%] on treatment with dry dioxan gave crystals containing 7·60% of zirconium.

We thank the Council of Scientific and Industrial Research for a research grant and an assistantship (to R. N. K.), and Messrs. Magnesium Elektron Ltd., London, for a gift of zirconium tetrachloride.

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77. *Chemical Applications of Nuclear Quadrupole Resonance Spectroscopy. Part II.*[1] *Chloro-derivatives of Maleic Anhydrides, Thiophen, and Anilinium Salts.*

By M. J. S. DEWAR and E. A. C. LUCKEN.

Measurements of chlorine nuclear quadrupole resonance frequencies are reported for *p*-chloroanilinium chloride and bromide, for mono- and dichloromaleic anhydrides, and for 2-chloro-, 2 : 5-dichloro, and 2 : 3 : 4 : 5-tetrachlorothiophen. The results are discussed in terms of hydrogen bonding in the *p*-chloroanilinium salts, carbon–chlorine π-bonding in the maleic anhydrides, and inductive effects in thiophen due to an increased electronegativity of sulphur, brought about by promotion of a 3*p* electron to a 3*d* orbital in forming the appropriate valence state.

IN Part I [1] we described a study of inductive and conjugative effects in chloro-derivatives of nitrogen heterocycles by nuclear quadrupole resonance spectroscopy; here we describe some further studies of compounds containing chlorine attached to unsaturated carbon atoms.

EXPERIMENTAL

The chlorine resonances were observed as described in Part I.[1] Chlorothiophens were prepared by chlorination of thiophen and separated by fractional distillation.[2] *p*-Chloroanilinium chloride and bromide were prepared from *p*-chloroaniline and the corresponding acid and recrystallised from dilute hydrochloric or hydrobromic acid. Monochloromaleic anhydride (a commercial specimen) and dichloromaleic anhydride (supplied by Imperial Chemical Industries Limited) were used without further purification.

The observed frequencies are shown in the Table.

Observed nuclear quadrupole resonance frequencies.

Compound	Frequency (Mc./sec.) 86° K	195° K	Room temp.
p-Chloroanilinium chloride	35·448	35·201	34·939 (297°)
p-Chloroanilinium bromide	34·752	34·636	34·440 (297°)
Chloromaleic anhydride	37·159	36·750	36·283 (297°)
Dichloromaleic anhydride	37·945, 38·013	37·565, 37·593	37·049, 37·065 (297°)
2-Chlorothiophen	A series of medium intensity lines in the region 34—39 Mc/sec.		
2 : 5-Dichlorothiophen	36·669 36·875		
	36·696 37·046		
	36·840 37·078		
2 : 3 : 4 : 5-Tetrachlorothiophen	37·517 38·500		36·906, 36·931
			37·740 (294°)

[1] Part I, Dewar and Lucken, *J.*, 1958, 2653.
[2] Conrad, Hartough, and Johnson, *J. Amer. Chem. Soc.*, 1948, **78**, 2564.

Discussion

It is necessary to decide to what extent it is legitimate to ascribe to purely electronic effects the differences in nuclear quadrupole resonance frequencies between different molecules, when it is known that electrostatic crystalline fields can cause an unpredictable lowering of frequency of up to several megacycles/sec. from that of the molecule in the gas phase.[3]

The number of molecules whose nuclear quadrupole coupling frequencies have been measured by microwave spectroscopy as well as by direct nuclear quadrupole resonance is unfortunately so small that no general conclusions can be drawn. It is therefore profitable to consider those compounds in which multiple resonances occur and in which no extraordinary factor, such as hydrogen-bonding, can account for this multiplicity. Results for compounds as varied as the Group IV tetrachlorides [4] and the polychlorobenzenes [5] show that splittings of up to 0·6 Mc./sec. are possible although in most cases they are not greater than 0·3 Mc./sec. A further indication of magnitude of solid-state effects can be obtained from the correlation between the Hammett function and the nuclear quadrupole resonance frequencies of substituted chlorobenzenes where the standard deviation between observed resonance frequencies and those predicted by the linear relationship derived by Bray and Barnes [6] is 0·36 Mc./sec. These facts, in conjunction with the success of pure quadrupole resonance measurements in demonstrating inductive effects in the alkyl halides,[4] indicate that a difference of more than 0·5 Mc./sec. between the chlorine nuclear quadrupole frequencies of two molecules is very probably due to electronic effects. This " limit of confidence " is considerably reduced when comparisons are being made between two *series* of different molecules.

The chlorine nuclear quadrupole resonance frequencies for the two salts of *p*-chloroaniline are much higher than that for the free base [7] (34·146 Mc./sec. at 77° K). Protonation of the amino-group can have several consequencies: (*a*) protonation will destroy the conjugative ($-E$) effect of the nitrogen which normally leads to an increased π-electron density at the *para*-carbon atom; (*b*) protonation will increase the inductive ($+I$) effect of nitrogen, and the resulting polarisation of the π-electrons will decrease the charge density at the *para*-carbon atom; (*c*) the increased electronegativity of nitrogen on protonation will, by a relayed (inductoelectromeric [8]) effect, increase the degree of π-bonding between chlorine and the ring. Now effects (*a*) and (*b*) will lead to a decrease in negative charge at the *para*-carbon atom, and so to a decrease in σ-bond polarity of the C–Cl bond and a consequent increase in nuclear quadrupole resonance frequency; effect (*c*) will lower [1] this frequency. The observed frequencies imply that the former effects predominate.

It is interesting that the frequencies for the two salts differ markedly, that for the hydrochloride being much the greater. This difference is most probably due to differences in hydrogen-bonding between the ammonium groups and halide anions in the salts. Such hydrogen-bonding will reduce the effective positive charge at the nitrogen atom and so lower its electronegativity; the argument of the previous section implies that there should be a corresponding increase in polarity of the C–Cl σ-bond, and a corresponding decrease in π-bonding between chlorine and the ring. Since the former effect will raise, and the latter lower, the quadrupole resonance frequency, one cannot be sure what the net effect will be. One cannot tell from the observed frequencies whether hydrogen-bonding is greater in *p*-chloroanilinium chloride or in the bromide—only that there must be a difference. We are investigating this problem further, for such measurements offer a most interesting method for studying hydrogen bonds in such salts.

[3] Allen, *J. Phys. Chem.*, 1953, **57**, 502.
[4] Livingstone, *J. Phys. Chem.*, 1953, **57**, 496.
[5] Bray, Barnes, and Bersohn, *J. Chem. Phys.*, 1956, **25**, 813.
[6] Bray and Barnes, *J. Chem. Phys.*, 1957, **27**, 551.
[7] Heal, *J. Amer. Chem. Soc.*, 1952, **74**, 6121.
[8] Brown and Dewar, *J.*, 1953, 2406.

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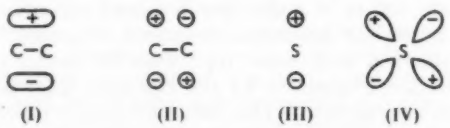
The frequencies of the mono- and di-chloromaleic anhydrides can be predicted approximately as follows. The frequencies at 20° K for vinyl chloride [9] (33·6 Mc./sec.) and for *cis*-dichloroethylene [4] (35·0 Mc./sec.) are known; the frequencies at 87° K will be about 0·2 Mc./sec. lower. The effect of the α-carbonyl group in the anhydride can be estimated approximately from the difference (2·3 Mc./sec.) between the nuclear quadrupole resonance frequencies for chloroacetic acid [3] and methyl chloride; [4] and that of the β-carbonyl group from the corresponding difference (1·8 Mc./sec.) between *o*-chlorobenzoic acids and chlorobenzene.[6] Together, these comparisons suggest that the nuclear quadrupole resonance frequency for a chloromaleic anhydride should be 2·3 + 1·8 = 4·1 Mc./sec. greater than that for the corresponding chloroethylene. The predicted frequencies for mono- and di-chloromaleic anhydride at 86° K are therefore 37·5 Mc./sec. and 38·9 Mc./sec. respectively, values which are greater than those observed (37·2 and 38·0 Mc./sec. respectively). These differences suggest that C–Cl π-bonding is greater in the anhydrides, for such π-bonding lowers the frequency; this is what one might expect in view of our work on chloro-derivatives of heterocycles, for the more electrophilic character of the C=C bond in maleic anhydride should lead to an increase in π-bonding to chlorine.

The frequencies of the thiophen compounds are interesting in that they seem to be much higher than those for the corresponding benzene derivatives (chlorobenzene, 34·622 Mc./sec.; *p*-dichlorobenzene, 34·779 Mc./sec.; 1 : 2 : 3 : 4-tetrachlorobenzene, 37·557, 37·455, 37·013 Mc./sec.).[5] This is surprising, for sulphur and carbon are thought to have closely similar electronegativities (2·5 on the Pauling scale). The difference cannot reasonably be ascribed to decreased π-bonding in the chlorothiophens, for since vinyl chloride has a lower frequency (33·4 Mc./sec.) than chlorobenzene, any decrease in aromatic character in thiophen as compared with benzene should if anything lower the nuclear quadrupole resonance frequency.

The electronic structure of thiophen has been discussed by Longuet-Higgins,[10] whose conclusions may be briefly summarised: The π-molecular orbitals of benzene can be written as combinations of six ethylenic π-molecular orbitals, three bonding and three antibonding, whose symmetries are indicated in (I) and (II); the resulting molecular orbitals are identical with those given by the usual LCAO approach. Likewise the π-molecular orbitals of thiophen can be constructed from a set of six orbitals, two pairs of ethylenic π-molecular orbitals and a pair of sulphur orbitals, 3*p* (III) and 3*d* (IV).



(I) (II) (III) (IV)

It is obvious from this diagram that the sulphur atomic orbitals resemble the ethylenic π-molecular orbitals in symmetry; they also have similar dimensions and binding energies. This representation therefore explains very clearly the close resemblance between benzene th ophen. As a result the π-electrons are uniformly shared between the six orbitals, so that the mean π-electron charge density is unity at each carbon atom and two at sulphur. This argument suggests that any differences between benzene and thiophen in π-electron distribution at the carbon atoms are small; the differences in nuclear quadrupole resonance frequencies for the chloro-derivatives cannot therefore be explained in terms of π-electron distributions.

However, this analysis requires the sulphur atom in thiophen to be in an excited valence state, with one 3*p* electron promoted into a 3*d* orbital. Since the screening effect of 3*d* electrons is small, the effective electronegativity of sulphur, as regards the 3*s* and 3*p* electrons,

[9] Livingstone, *J. Chem. Phys.*, 1951, **19**, 1613.
[10] Longuet-Higgins, *Trans. Faraday Soc.*, 1949, **45**, 173.

will be increased; indeed, Slater's rules imply an increase in effective nuclear charge of 0·35 unit for the 3*s* and 3*p* electrons. This will lead to a strong inductive polarisation (C ⟶ S) of the C–S σ-bond, formed by a 3*s*–3*p* orbital, and this by a relayed inductive effect will lead a decreased σ-bond polarity (and increased nuclear quadrupole resonance frequency) for the C–Cl bonds in the chlorothiophens.

A similar change in electronegativity must occur in other compounds where sulphur atoms use *d* orbitals to form bonds; the very strong inductive effect of the sulphonyl group may be due largely to this.

Since the publication of Part I, our attention has been drawn to the paper by Kojima *et al.*[11] in which piezoelectric resonances in a variety of inorganic compounds were reported. The radiofrequency spectra here observed consisted of a series of sharp resonances occurring over a considerable frequency range—some tens of megacycles— and in which one or more series obeying an interval-rule could be detected. It is probable that the multiple resonances of 2 : 4 : 6-trichloropyrimidine and of 2-chlorothiophen should be ascribed to this cause rather than to any randomness in the orientation of molecules in the crystal.

We thank the Royal Society and the University of London for grants for the purchase of apparatus, and Imperial Chemical Industries Limited for a loan of dichloromaleic anhydride. One of us (E. A. C. L.) thanks the Department of Scientific and Industrial Research for a maintenance grant.

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LONDON, E.1. [*Received, May 21st,* 1958.]

[11] Kojima, Tsukada, Ogawa, and Shimauchi, *J. Phys. Soc. Japan*, 1955, **10**, 265.

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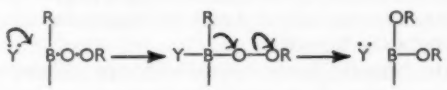
78. *Peroxides of Elements other than Carbon. Part III.* The Formation of Boron Peroxides by Autoxidation.*

By M. H. ABRAHAM and ALWYN G. DAVIES.

The autoxidation of tri-*n*-butylboron and of a mixed *tert.*- and *iso*-butylboron has been investigated. It is shown that the primary reaction is represented by $R{-}B\lessgtr + O_2 \longrightarrow R{\cdot}O{\cdot}O{\cdot}B\lessgtr$, and from the latter the product $BuB(OBu)_2$ has been isolated.

If the oxygen supply is restricted, excess of the trialkylboron reduces the peroxy-group, and the boronic ester $RB(OR)_2$ is the ultimate product.

Nucleophilic attack by water or by pyridine at the boron atom in compounds containing the structure $RB{\cdot}O{\cdot}OR$ induces nucleophilic rearrangement with displacement of the alkyl group from boron to oxygen:



If the reagent Y is a peroxyacid, this is reduced preferentially.

It is suggested that the autoxidation of the alkylboron compounds proceeds through a mechanism involving co-ordination of molecular oxygen to the boron atom, and a shift of the alkyl group from boron to oxygen.

IN Part I [1] it was pointed out that the peroxide group could be introduced into an organic molecule by the nucleophilic reaction of a peroxidic reagent, or by a reaction involving

* Part II, *J.*, 1958, 2372. A preliminary account of the present work has appeared in *Chem. and Ind.*, 1957, 1622.

[1] Buncel and Davies, *J.*, 1958, 1550.

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molecular oxygen, and we have described an extension of the former reaction to the preparation of organoperoxy-silicon [1] and -boron [2] compounds. This paper is the first of a number which will describe the preparation of peroxides of elements other than carbon by autoxidation.

Autoxidation of Organometallic Compounds.—Many metal and metalloid alkyls react with molecular oxygen, frequently with inflammation. For reaction to occur readily, the element must apparently have an unoccupied orbital of low energy and, within any one Sub-group, the reactivity can be correlated with the Pauling-scale electronegativity of the element (except possibly for the zinc and cadmium alkyls).[3]

It might be expected that the initial product of the autoxidation of an organo-element compound would generally retain intact a single O–O bond,[4] as it does in the autoxidation of a purely organic compound. However, the organometallic and organometalloid compounds are frequently strong reducing agents and under the usual conditions of autoxidation they might reduce the initial peroxides to non-peroxidic compounds:

$$RM + O_2 \longrightarrow RMO_2 \xrightarrow{RM} 2RMO$$

The literature supports this: whereas non-peroxidic products have usually been isolated, the presence of traces of oxidising material has frequently been reported.[5] Walling and Buckler recently [6] showed that adding an ethereal solution of a Grignard reagent to oxygen-saturated ether at −80° gives high yields of the corresponding peroxides. Excess of the Grignard reagent reduces these peroxides to the alkoxides:

$$R{\cdot}MgX + O_2 \longrightarrow [RO{\cdot}OMgX] \begin{cases} \xrightarrow{H_2O} RO{\cdot}OH \\ \xrightarrow[R{\cdot}MgX]{} 2RO{\cdot}MgX \end{cases}$$

Autoxidation of Alkylboron Compounds.—In this field we have investigated first the autoxidation of the alkylboron compounds because we have already prepared a number of organo-peroxyboron compounds from alkyl hydroperoxides.[2]

Trialkylborons are rapidly autoxidised and the lower members inflame in the air. From the controlled oxidation, dialkyl alkylboronates have been obtained, and this reaction has been used to prepare several boronic acids:

$$R_3B + O_2 \longrightarrow RB(OR)_2 \xrightarrow{H_2O} RB(OH)_2 + 2ROH$$
$$(R = Et,[7]\ Pr,[8]\ Pr^i,[9]\ Bu,[10]\ Bu^i,[8]\ Bu^t,[9]\ CH_2Bu^i\ [8])$$

This formation of boronic esters was confirmed by Johnson and van Campen [10] who showed that tri-*n*-butylboron took up one mol. of oxygen to give the boronate, $BuB(OBu)_2$. In the presence of water, however, only 0·5 mol. of oxygen was absorbed and the boronite, $Bu_2B(OBu)$, was reported to be formed.

In the vapour state trimethylboron reacts with one volume of oxygen to give one

[1] Davies and Moodie, *J.*, 1958, 2372.
[2] Frankland, *J.*, 1861, **13**, 177; M. H. Abraham, Thesis, London, 1957; see also Sanderson, *J. Amer. Chem. Soc.*, 1955, **77**, 4531; Gilman and Jones, *ibid.*, 1940, **62**, 2353.
[3] Gilman, Yablunky, and Svigoon, *ibid.*, 1939, **61**, 1170; Egerton and Rudrakanchana, *Proc. Roy. Soc.*, 1954, *A*, **225**, 427.
[4] *E.g.*, Frankland, *Annalen*, 1855, **95**, 46; Meyer and Demuth, *Ber.*, 1890, **23**, 394; Engler and Wild, *ibid.*, 1897, **30**, 1669; Engler and Weissberg, *ibid.*, 1898, **31**, 3055.
[5] Walling and Buckler, *J. Amer. Chem. Soc.*, 1953, **75**, 4372; 1955, **77**, 6032.
[6] Meerwein and Sönke, *J. prakt. Chem.*, 1936, **147**, 251; Frankland, *J.*, 1862, **15**, 363; *Annalen*, 1862, **124**, 129.
[7] Krause and Nitsche, *Ber.*, 1921, **54**, 2784.
[8] Krause and Nobbe, *Ber.*, 1931, **64**, 2112.
[9] Johnson and van Campen, *J. Amer. Chem. Soc.*, 1938, **60**, 121.

volume of product which was assigned the probable structure $MeB(OMe)_2$. Tri*iso*propylboron reacts similarly, but the boronate may undergo further slow oxidation to the borate.[11] While the present work was being carried out, Petry and Verhoek [12] described the oxidation of trimethylboron with a two-fold excess of oxygen in a flow system with a contact time of 2—3 min. at room temperature and 10—15 mm. Largely on the basis of physical evidence they assign their product the structure $Me_2B{\cdot}O{\cdot}OMe$.

Most dialkylboron compounds such as Bu_2BCl and $Bu_2B{\cdot}O{\cdot}BBu_2$ are also rapidly oxidised by air.[13] The controlled autoxidation of the spontaneously inflammable diethylboronous acid and ethyl diethylboronite has been reported to proceed as follows: [14]

$$Et_2B{\cdot}OH + \tfrac{1}{2}O_2 \longrightarrow Et{\cdot}B(OH){\cdot}OEt$$
$$Et_2B{\cdot}OEt + \tfrac{1}{2}O_2 \longrightarrow Et{\cdot}B(OEt)_2$$

Monoalkylboron compounds are much more stable towards oxygen.[15] Except for the tertiary and secondary alkylboron difluorides, which may ignite in the air, the alkylboron dihalides are unaffected by oxygen. Boronic esters are also stable, but the boronic acids are susceptible to oxidation. Secondary and especially tertiary alkylboronic acids are rapidly autoxidised, but water completely inhibits the reaction of the primary and secondary compounds.[16] The trimeric boronic anhydrides, $(RBO)_3$, are oxidised quantitatively to the metaborates—tertiary ones very rapidly and primary ones only slowly. Evidence was found for a peroxidic intermediate which liberated iodine from potassium iodide and initiated the polymerisation of styrene,[17] and was thought to be

$$Bu{-}B{=}O$$
$$\uparrow$$
$$O_2$$

The alkenyl- and aryl-boron compounds are relatively much more stable. Triphenylboron in 1-bromonaphthalene reacts with ½ mol. of oxygen fairly rapidly at room temperature to give presumably the phenylboronite. Under the same conditions tri-1-naphthylboron is much less reactive, and trimesitylboron is inert.[18] Trivinylboron similarly shows no reactivity at room temperature, but methyldivinylboron is more reactive.[19]

Diarylboron compounds have been reported to become brown on exposure to air,[20] but monoarylboron compounds are stable.[21]

Formation of Alkylperoxyboron Compounds by Autoxidation.—(i) *From tri-*n*-butylboron.* The autoxidation of tri-*n*-butylboron was studied first because this had been most extensively investigated.[10] In the gas burette in the absence of a solvent, tri-*n*-butylboron absorbed 1·01 mol. of oxygen, giving a product with properties corresponding to those of dibutyl butylboronate, but containing a trace (0·02 mol.) of a peroxidic compound (iodometrically).

However, a solution of tri-*n*-butylboron in *cyclo*hexane absorbed much more than 1 mol. of oxygen, producing just over 1 mol. of oxidising agent. The product was diamagnetic and in solution did not lose its oxidising properties to an appreciable extent during some days. Tributylboron, if added at the end of the autoxidation or if in excess during the autoxidation, reduced the oxidising product to dibutyl butylboronate.

A reasonable interpretation of this behaviour might be that autoxidation of R_3B gives initially $R_2B{\cdot}O{\cdot}OR$ which can be reduced by an R–B group giving $R_2B{\cdot}OR$, or can be

[11] Bamford and Newitt, *J.*, 1946, 695.
[12] Petry and Verhoek, *J. Amer. Chem. Soc.*, 1956, **78**, 6416.
[13] Johnson, Snyder, and van Campen, *ibid.*, 1938, **60**, 115.
[14] Frankland, *Proc. Roy. Soc.*, 1877, **25**, 165.
[15] McCusker and Glunz, *J. Amer. Chem. Soc.*, 1955, **77**, 4253.
[16] Snyder, Kuck, and Johnson, *ibid.*, 1938, **60**, 105; Johnson, van Campen, and Grummitt, *ibid.*, p. 111.
[17] Grummitt, *ibid.*, 1942, **64**, 1811.
[18] Brown and Dodson, *ibid.*, 1957, **79**, 2302.
[19] Parsons, Silverman, and Ritter, *ibid.*, p. 5091.
[20] Torssell, *Acta Chem. Scand.*, 1955, **9**, 239.
[21] *Idem, ibid.*, 1954, **8**, 1779.

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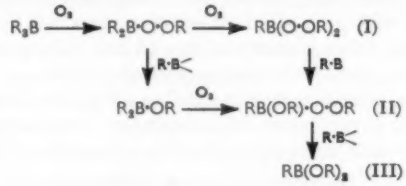
further oxidised by oxygen to $RB(O{\cdot}OR)_2$. The final product might therefore be (I), (II), or (III), depending on the conditions:



In the present case the combination of these reactions has given a product consisting largely of (II; R = Bu). Hydrolysis of this (see below) might liberate *n*-butyl hydroperoxide but, as this forms no convenient crystalline derivatives, we have also investigated the autoxidation of the *tert.*-butylboron group because *tert.*-butyl hydroperoxide is relatively stable and forms familiar crystalline derivatives.

(ii) *From* " tert.-*butylboron.*" Tri-*tert.*-butylboron (if indeed it exists) is unstable and partial rearrangement occurs to the *iso*butyl structure.[22] Oxidation of our product with hydrogen peroxide followed by estimation of the *iso*- and *tert.*-butyl alcohol formed showed our alkyl to contain an average of about 0·80 *iso*butyl group per molecule. We refer to this mixed alkyl as " *tert.*-butylboron." *

As in the case of the *n*-butyl compound, " *tert.*-butylboron " in concentrated *cyclo*hexane solution absorbed 1·01 mol. of oxygen giving a product containing only 0·04 mol. of peroxide. Hydrolysis gave a solid, m. p. 105°, which could be either *tert.*- or *iso*-butylboronic acid. (The structure of Krause and Nobbe's " *tert.*-butylboronic acid,"[9] is rendered unreliable by the above isomerisation.) Apart from the ambiguity of isomerisation, however, the oxidation can again be expressed as $R_3B + O_2 \longrightarrow RB(OR)_2$.

In dilute ethereal solution, however, the alkyl absorbed much more oxygen, giving highly peroxidic products. By bubbling oxygen through a very dilute ethereal solution, a product containing 1·94 mol. of peroxidic oxygen was obtained, and was isolated as a clear colourless oil, giving an analysis agreeing satisfactorily with the structure $BuB(O{\cdot}OBu)_2$. In a thin film the oil was hydrolysed very rapidly forming a white crust of boric acid and giving a characteristic peroxidic odour.

Hydrolysis of the Autoxidation Products.—Initial experiments to detect *n*-butyl hydroperoxide in the hydrolysate of the compound $Bu^nB(OBu^n){\cdot}O{\cdot}OBu^n$ were not successful, and under conditions under which the hydroperoxide and *n*-butylboronic acid are stable only *n*-butyl alcohol and boric acid could be recovered.

Similar loss of peroxide occurred during the hydrolysis of the oxidation products of " *tert.*-butylboron," but was incomplete when the initial peroxide content was greater than 1 mol. In the hydrolysate, *tert.*-butyl hydroperoxide was identified on the vapour-phase chromatogram, and isolated as its triphenylmethyl derivative. This therefore confirms that the autoxidation can be expressed by the reaction, $R_3B + 2O_2 \longrightarrow RB(O{\cdot}OR)_2$.

The loss of peroxide, and the accompanying formation of boric acid and alcohol during the hydrolysis of compounds containing the structure $\overset{|}{R}B{\cdot}O{\cdot}OR$, was surprising. Further investigation showed (Table 2) that the peroxide content decreased from $1 + n$ to n groups

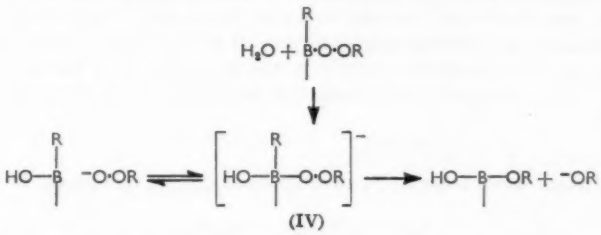
* In a recent thorough investigation,[23] Hennion, McCusker, and Rutkowski isolated only di*iso*butyl-*tert.*-butylboron by three different routes which might be expected to give tri-*tert.*-butylboron, including the one which we have followed. We would not exclude the possibility that our alkyl contained an average of more than one *iso*butyl group per molecule, although we think it is unlikely; our general argument, however, does not depend on this fact.

[22] Hennion, McCusker, Ashby, and Rutkowski, *J. Amer. Chem. Soc.*, 1957, **79**, 5190.
[23] Hennion, McCusker, and Rutkowski, *ibid.*, 1958, **80**, 617.

per boron atom. This reaction is reminiscent of the oxidative dealkylation of organoboron compounds by hydrogen peroxide and by alkyl hydroperoxides. Kuivila has shown kinetically that this rearrangement proceeds through a four-covalent boron intermediate,[24] and our experiments [2] with phenyl[^{18}O]boronic acid and with optically active 1-phenylethyl hydroperoxide support his conclusions.

It therefore appears that the dealkylation and loss of peroxide content which we observe on hydrolysis result from a similar rearrangement in the intermediate (IV).

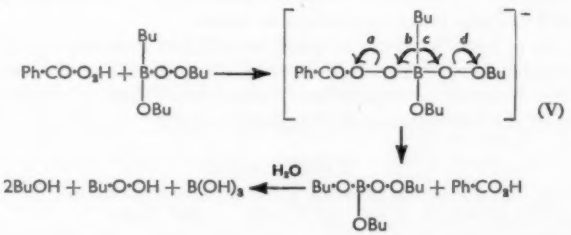
This type of rearrangement prevented the preparation of compounds of the type RB(OH)·O·OR by the nucleophilic substitution of a hydroperoxide at a boron atom, a reaction which would also proceed through a four-covalent intermediate.[2]



(IV)

Similar oxidative dealkylation occurred when the organoperoxyboron compounds were treated with pyridine or piperidine. It appears that the reaction is now induced by nucleophilic attack of the amine upon boron.

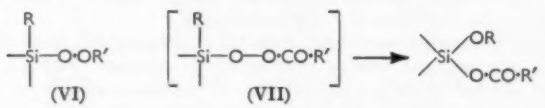
The reaction of the peroxide from tri-*n*-butylboron with peroxybenzoic acid supports this mechanism:



(V)

The alkyl group now can migrate in either of two directions, involving the electron shifts *a* and *b*, or *c* and *d* (structure V); the former is favoured by electron-attraction in the benzoyloxy-group. Rearrangement therefore leads to the formation of benzoic acid; hydrolysis liberated *n*-butyl hydroperoxide, identified by comparison with an authentic specimen on the vapour-phase chromatogram.

We have obtained a similar relative mobility in the acylperoxy- and alkylperoxy-derivatives of silicon.[1] Whereas no rearrangement could be induced in structures of the type (VI), the structure (VII) was too unstable to be isolated.



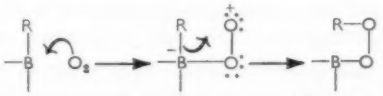
(VI) (VII)

Nature of the Autoxidation Process.—The autoxidation of tri-*n*-butylboron was inhibited in propylamine solution. In aqueous emulsion "*tert.*-butylboron" absorbed 1·21 mol. of

[24] Kuivila, *J. Amer. Chem. Coc.*, 1954, **76**, 870; Kuivila and Armour, *ibid.*, 1957, **79**, 5659.

oxygen and gave (in a separate experiment) a product containing 0·33 mol. of peroxide. Quinol in small amount has no effect on the rate or overall uptake of oxygen.

A reasonable interpretation of these results, and those of previous workers quoted above, is that the autoxidation proceeds by co-ordination of molecular oxygen on to the boron atom, accompanied or followed by a 1 : 3-shift of the alkyl group from boron to oxygen:



Consonant with this, a general parallel can be traced between the ease of autoxidation of organoboron compounds and the readiness with which other reagents co-ordinate to the boron atom, modified by the migratory aptitude of the group R. Any group which can donate electrons inter- or intra-molecularly to the unfilled shell of the boron atom will by doing so render the compound less susceptible to attack by oxygen. For example the reactivity series

$$\text{Alkyl-B}\lessdot > \text{Vinyl-B}\lessdot \sim \text{Aryl-B}\lessdot$$

on this picture might arise from p_π–p_π overlap from the organic group to boron, and the series

$$\begin{aligned} R_3B &> R_2B{\cdot}OR > RB(OR)_2 \\ R_2B{\cdot}OH &> R_2B{\cdot}OR > R_2B{\cdot}O^-Na^+ \\ R_2B &> R_2BCl > RBCl_2 \end{aligned}$$

from a similar overlap from the oxygen or halogen atoms.

The inhibition of the autoxidation of tributylboron by propylamine, and of the less reactive boronic acids by water, can perhaps be ascribed to the successful competition of these reagents with oxygen for co-ordination to boron.

The mechanism of autoxidation discussed here differs from that proposed by Bamford and Newitt for the reaction of trimethyl- and tripropyl-boron in the vapour phase,[11] and by Coates for the reaction of organozinc compounds,[25] but is similar to Walling and Buckler's picture of the autoxidation of Grignard reagents.[6]

Experimental

Tri-n-*butylboron*.—The reaction between *n*-butylmagnesium bromide and boron trifluoride in ether gave tri-*n*-butylboron, b. p. 96—98°/12 mm., in 59% yield.

" tert.-*Butylboron*."—This material, b. p. 66—68°/7 mm., was prepared similarly in 45% yield (on BF_3) from *tert.*-butylmagnesium chloride (Found: B, 5·91. Calc. for $C_{12}H_{27}B$: B, 5·90%). A solution of this material (4·55 g.) in *cyclo*hexane (4 c.c.) was shaken for 2 hr. with 30% hydrogen peroxide (10 c.c.), with ice-cooling. The mixture was kept overnight at room temperature, then treated with more hydrogen peroxide (5 c.c.), made alkaline with potassium hydroxide, and shaken for a further 1·5 hr. Potassium carbonate was added, the mixture extracted with ether, and the extract dried and concentrated through a Dufton column to 11·05 g. This extract was then treated as follows.

(i) On the vapour-phase chromatogram, comparison of the area of the *iso*butyl alcohol peak with those for *cyclo*hexane and for ether, both for the extract alone and for a mixture of the extract (0·1980 g.) and *iso*butyl alcohol (0·0452 g.), showed that 0·79 mol. of *iso*butyl alcohol had been isolated from the oxidation of " *tert.*-butylboron."

(ii) By a carefully controlled procedure, *iso*butyl 3 : 5-dinitrobenzoate (0·87 g.), m. p. and mixed m. p. 86·2°, was isolated from a portion of the extract (3·66 g.). By an identical procedure, *iso*butyl alcohol (0·50 g.) yielded the 3 : 5-dinitrobenzoate, m. p. 86° (0·87 g.); about 0·82 mol. of *iso*butyl alcohol had therefore been isolated from the oxidation.

Preparation of Capsules.—The boron alkyl was introduced under nitrogen through the B10 side-arm *A* (Fig. 1) which could be connected directly to the distillation apparatus. In a nitrogen-filled glove-box, the weighed, thin, glass capsules *B*, ending in a narrow capillary and filled

[25] Coates, " Organo-metallic Compounds," Methuen, London, 1956, p. 39.

with nitrogen, were inverted in the neck of the apparatus and the B29 cap *C* replaced. The pressure in the apparatus was reduced through *D*, and nitrogen readmitted through *E*. The capsules were removed in the wire stirrup *F* while they were still under reduced pressure so that the capillaries filled with nitrogen. The capsules were then sealed and reweighed.

Autoxidations.—Fig. 2 illustrates the apparatus found most convenient for carrying out the autoxidations. The capsule *A* was placed in the solvent *B* with the capillary neck in the arm of the tap *C* which enters the swan-neck adapter through a rubber sleeve. The adapter leads to the gas burette and the dimethyl phthalate bubbler through the three-way tap *D*.

Oxygen was passed in through *C* and out at *D*, and the mercury reservoir was lowered to fill the burette with oxygen. Taps *C* and *D* were then closed to the atmosphere, and when the apparatus had reached thermal equilibrium the capsule was crushed by depressing the tap *C*, the mixture being stirred magnetically. Further liquid reagents can be added if necessary through the tap *C*.

FIG. 1. *Apparatus for filling capsules.*

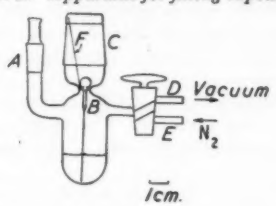
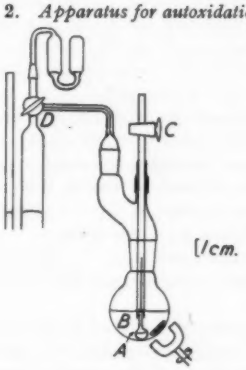


FIG. 2. *Apparatus for autoxidations.*



Determination of Boron.—The sample (0·1—0·2 g.) was added to 30% hydrogen peroxide (10 c.c.). After 2—3 hr., mannitol (1·0 g.) was added, and the solution was titrated with 0·1N-sodium hydroxide with phenolphthalein as indicator. A blank estimation was run concurrently. Use of Bromothymol Blue gives a better end-point and smaller blank estimations (Dr. M. F. Lappert, personal communication), and we used this in subsequent work.

Vapour-phase Chromatographic Analysis.—The general method has already been described.[24] Preliminary identification of compounds was based on the retention times (*T*), relative to *tert.*-butyl peroxide, which are given in Table 1; this was followed by adding an authentic sample of the suspected component to the mixture, and redetermining the chromatogram.

Quantitative analysis was based on the measurement of the areas under curves, determined by weighing a cut-out replica. Values of *F* (*tert.*-butyl peroxide = 1), defined by the expression

$$\frac{\text{Area of A}}{\text{Area of B}} \times F\frac{\text{A}}{\text{B}} = \frac{\text{Wt. of A}}{\text{Wt. of B}}$$

are given in Table 1.

TABLE 1. *Vapour-phase chromatographic analysis.*

Packing: dinonyl phthalate on kieselguhr. Temp.: 80—85°. Carrier gas: N_2, 3·95 l./hr.

	H_2O	Et_2O	Me_2CO	Bu^t·OH	Pr^i·CHO	Pr^n·CHO
T	0·18	0·22	0·31	0·46	0·46	0·68
F	—	—	—	0·199	—	0·135
	$Bu^t_2O_2$	Bu^i·OH	Bu^n·OH	Bu^t·O_2H	Bu^i·O_2H	Bu^n·O_2H
T	1·00	1·16	1·170	2·77	4·82	6·50
F	1·00	0·158	0·135	1·53	0·272	0·303

Autoxidation of Tri-n-butylboron.—(i) *With no solvent.* Tri-*n*-butylboron (2·2762 g.) was allowed to absorb oxygen in the gas burette, the temperature being kept below 20—25° by

[24] Abraham, Davies, Llewellyn, and Thain, *Analyt. Chim. Acta*, 1957, **17**, 499.

XUM

intermittent cooling. 1·01 Mol. of oxygen were absorbed, giving a product (2·647 g. Calc.: 2·676 g.) containing 0·02 mol. of peroxide, b. p. 119°/23 mm., n_D^{20} 1·4171, n_D^{25} 1·4150. Recorded data for di-*n*-butyl butylboronate are b. p. 108·5°/13 mm., n_D^{20} 1·4169.

Partial hydrolysis (of 1·626 g.) occurred with 6N-hydrochloric acid (5 c.c.) in 5 hr., giving boric acid (0·03 g.), m. p. and mixed m. p. 165—166°, and *n*-butyl alcohol (0·10 g.) (3 : 5-dinitrobenzoate, m. p. 58—59°, unchanged on admixture with authentic material, m. p. 64°).

(ii) In *cyclo*hexane. Tri-*n*-butylboron (0·4648 g.) in *cyclo*hexane (5 c.c.) absorbed 1·21 mol. of oxygen in 1 hr., giving a product containing 1·06 mol. of peroxide.

(iii) *Reduction of the product by the reactant.* Tri-*n*-butylboron (0·6340 g.) in *cyclo*hexane (7·0 c.c.) absorbed oxygen, giving a product (5·7842 g. in all) containing 0·71 mol. of peroxide. This solution (5·1383 g., containing $3·98 \times 10^{-3}$ mole of peroxide) was mixed with a solution of the trialkyl (0·7263 g., $3·98 \times 10^{-3}$ mole) in *cyclo*hexane (3·0 c.c.), heat being evolved. After being kept overnight under nitrogen, the solution was allowed to absorb oxygen, and gave a product containing $0·76 \times 10^{-3}$ mole of peroxide. Di-*n*-butyl *n*-butylboronate (0·58 g.) was isolated, having b. p. 124—127°/26 mm., n_D^{25} 1·4148 [Found: C, 65·7 (uncorr.); H, 12·4. Calc. for $C_{12}H_{27}O_2B$: C, 67·4; H, 12·6%].

(iv) *Stability of the peroxide.* The trialkylboron (3·667 g.) in *cyclo*hexane (40 c.c.) was allowed to absorb oxygen. Next day the solution was diluted to 50 c.c. with *cyclo*hexane. Aliquot portions showed the following peroxide contents (in mol.): initially, 0·51; after 6 hr./35°, 0·47; after 6 hr./53°, 0·41; after 3 days/20°, 0·43.

(v) *Oxidation with a restricted oxygen supply.* The trialkylboron (0·6980 g.) in *cyclo*hexane (10 c.c.) was allowed to absorb 0·55 mol. of oxygen in a few minutes. The supply of oxygen was then interrupted at tap *D*. Next day the oxygen supply was restored. The final product contained 0·31 mol. of peroxide.

(vi) " *Inverse oxidation.*" The trialkylboron (0·9702 g.) in *cyclo*hexane (50 c.c.) was added during 3·5 hr. to *cyclo*hexane (25 c.c.) stirred in dry oxygen. The product contained 0·783 mol. of peroxide.

Autoxidation of " tert.-*Butylboron.*"—(i) *In* cyclo*hexane.* The trialkyl (1·14 g.) in *cyclo*hexane (1·0 c.c.) absorbed 1·01 mol. of oxygen, giving a product containing 0·04 mol. of peroxide. Alkaline hydrolysis of the product under nitrogen gave a white solid (recrystallised from water), m. p. 105°.

(ii) *In ether.* The trialkylboron (0·1212 g.) in dry ether (3·3 c.c.) absorbed oxygen at room temperature during 3·5 hr., giving a product containing 1·79 mol. of peroxide. In a similar experiment at −70° for 9 hr., 1·26 mol. of peroxide were produced.

A solution of the trialkyl (6·30 g.) in dry ether (100 c.c.) was added slowly during 9 hr. to dry ether (250 c.c.) which was continuously saturated with dry oxygen and cooled in ice (" inverse oxidation "), giving a product containing 0·01 mol. of peroxide.

The ether was removed from 250 c.c. of the solution, leaving a clear liquid (1·21 g.), b. p. 38—40°/0·15 mm., n_D^{20} 1·4078, n_D^{25} 1·4056. This (1·0 g.) was shaken with 3N-sodium hydroxide (50 c.c.); *tert.*- and *iso*-butyl alcohol were identified in the ethereal extract of the steam-distillate.

The alkaline residue from the steam-distillate was concentrated and acidified under nitrogen, yielding a white solid (0·27 g.), m. p. 100° (after sublimation). Above the m. p. a liquid was evolved with an odour similar to that of *tert.*-butyl alcohol, leaving a residue of boric acid.

(iii) *Isolation of the product.* A capsule of the trialkyl (*ca.* 0·2 g.) was broken under dry ether (40 c.c.) through which oxygen was passed for 8 hr., and which was stirred magnetically. The combined products from five such reactions (total wt. of alkyl, 0·8204 g.) were filtered from glass in the dry box and shown to contain 1·94 mol. of peroxide.

The solvent was removed at the pump under anhydrous conditions, leaving *butyldi*(*butylperoxy*)*boron* as a clear colourless liquid (0·8501 g.) [Found: C, 55·9 (uncorr.); H, 11·0; B, 4·5; peroxidic O, 24·5. $C_4H_9B(O_2C_4H_9)_2$ requires C, 58·5; H, 11·1; B, 4·4; peroxidic O, 26·0%].

Hydrolysis of the Autoxidation Products.—n-*Butylperoxy-compounds.* An autoxidation product containing 1·14 mol. of peroxide in ether (250 c.c.) was hydrolysed as follows.

(i) *With acid.* A 100 c.c. aliquot part was concentrated and hydrolysed during 1 week with 6N-hydrochloric acid (10 c.c.), and the hydrolysis product (2·3580 g.) was collected in ether. The chromatogram showed the presence of *n*-butyl alcohol and a trace of *n*-butyraldehyde. Quantitative analyses by chromatography and by isolation of *n*-butyl 3 : 5-dinitrobenzoate

(m. p. 64°) were in good agreement, and showed that from the oxidation product containing 1·14 mol. of peroxide, 1·88 mol. of *n*-butyl alcohol had been isolated.

(ii) *With alkali.* A second 100 c.c. aliquot portion was similarly treated with 3N-sodium hydroxide (10 c.c.) for 5 hr. The clear liquid residue (1·8803 g.) from the ethereal extract contained 0·04 mol. of peroxide. Again the chromatogram showed the presence of only ether, *n*-butyl alcohol (2·38 mol.), and a trace of *n*-butyraldehyde.

(iii) *With peroxybenzoic acid.* A 12·5 c.c. sample of the solution was added to a solution of peroxybenzoic acid (1·0 g.) in dry ether (5 c.c.). Next day the mixture was shaken with water (0·5 c.c.) for 5 hr. and the material volatile at 0·1 mm. was collected in a trap at −80° as a clear liquid (0·445 g.). On the chromatogram peaks corresponding to *n*-butyl alcohol (2·09 ± 0·3 mol.), *n*-butyl hydroperoxide (0·57 ± 0·07 mol.), and *n*-butyraldehyde (0·44 ± 0·07 mol.) were identified. If it is assumed that the aldehyde is derived from the hydroperoxide, the combined yields of 1·01 mol., and that of the alcohol, *ca.* 2 mol., correspond satisfactorily with the peroxidic content, 1·14 mol. of the autoxidation product.

(iv) *With piperidine.* Tri-*n*-butylboron (0·9397 g.) in *cyclo*hexane (40 c.c.) was allowed to absorb oxygen for 6 hr., giving a product containing 0·50 mol. of peroxide. Piperidine (2·0 c.c.) was added, giving a slightly exothermic reaction. After 16 hr. at 40°, the solution gave a negative test for peroxide. To check that this was not due to base-catalysed decomposition of the primary alkyl peroxide, the solution was analysed for butyraldehyde as its 2 : 4-dinitrophenylhydrazone which was isolated by chromatography on alumina. The optical density of the product at 360 μ showed that a maximum of 4% of the *n*-butyl peroxide had been converted into the aldehyde.

tert.-*Butylperoxy-compounds.*—(i) *The products of hydrolysis.* An autoxidation product in ether containing 1·60 mol. of peroxide was shaken for 1 hr. with 6N-sodium hydroxide (5 c.c.) and then steam-distilled. The product was extracted into ether, and on the chromatogram showed the presence of *tert.*-butyl hydroperoxide, *iso*butyl alcohol, *tert.*-butyl alcohol, and a trace of acetone.

(ii) *Isolation of* tert.-*butyl triphenylmethyl peroxide.* "*tert.*-Butylboron" (0·2137 g.) in ether (6·0 c.c.) was allowed to absorb oxygen for 4 hr., giving a product containing 1·59 mol. of peroxide. The product was hydrolysed as above. Triphenylmethanol (0·08 g.) in glacial acetic acid (3·5 c.c.) containing sulphuric acid (2 drops) was added to the residue (0·5 c.c.). After 3 hr. the mixture was poured on ice, yielding *tert.*-butyl triphenylmethyl peroxide (0·045 g.), m. p. 71°, undepressed on admixture with authentic material,[27] m. p. 73°.

In a check experiment, a solution of *tert.*-butyl hydroperoxide (0·05 g.) in water (5·0 c.c.) by the same procedure yielded 0·06 g. of the triphenylmethyl derivative. About 0·36 mol. of hydroperoxide was therefore formed in the hydrolysis of the autoxidation product.

(iii) *Reaction with pyridine.* Four capsules of "*tert.*-butylboron" (in all, 0·4987 g.) were oxidised in ether, giving 100 c.c. of a solution of the product containing 1·94 mol. of peroxide. Dry pyridine (1 c.c.) was added. Next day the solvent was removed, leaving a compound containing 0·94 mol. of peroxide. After 3 weeks in contact with pyridine the peroxide content was 0·77 mol.

(iv) *Loss of peroxide during hydrolysis.* Various products from the autoxidation of "*tert.*-butylboron" were hydrolysed as described above, and the peroxide content was determined before and after hydrolysis. These results are recorded in Table 2. The values marked *s* were determined after steam-distillation and have been corrected for the loss of about 25% of peroxide which occurs during this process.

TABLE 2. *Loss of peroxide accompanying hydrolysis.*

Peroxide content (mol.)			Peroxide content (mol.)		
Before hydrolysis	After hydrolysis	Reagent	Before hydrolysis	After hydrolysis	Reagent
1·26	0·29	HCl	1·60	0·60	NaOH
1·50	0·55 *s*	NaOH	1·68	0·63 *s*	NaOH
1·59	0·48 *s*	NaOH	1·94	0·94	C_5H_5N

Effect of Reagents on the Autoxidation.—Water. "*tert.*-Butylboron" (0·0616 g.) in water (0·70 c.c.) absorbed 1·21 mol. of oxygen in 3 hr.

A vigorous stream of oxygen was passed through a suspension of "*tert.*-butylboron" in water (25 c.c.); after about 15 min. the mixture became homogeneous. After 7 hr. the aqueous solution and the contents of a subsequent trap at −70° were shown to contain 0·33 mol. of

XUM

peroxide. *tert.*-Butyl hydroperoxide and *iso*- and *tert.*-butyl alcohol were identified on the chromatogram.

Propylamine. " *tert.*-Butylboron " (0·0431 g.) in *n*-propylamine (4·5 c.c.) was left in contact with oxygen overnight. No measurements of the volume absorbed were possible because of the high vapour pressure of the system. The residual alkyl was therefore estimated by treating it with an excess of *tert.*-butyl hydroperoxide and determining the excess of hydroperoxide in the usual way: 2·49 of the original 3 alkyl groups were still available for reduction.

Quinol. " *tert.*-Butylboron " (0·3305 g.) and quinol (0·10 g.) in di*iso*propyl ether (5 c.c.) absorbed 1·22 mol. of oxygen in 6 hr. The quinol was recovered and no benzoquinone could be detected. In a parallel experiment the alkyl (0·3644 g.) in di*iso*propyl ether (5 c.c.) absorbed 1·28 mol. of oxygen at the same rate.

We are indebted to Dr. J. Artozoul for preparing the tri-*n*-butylboron. This work was carried out during the tenure of a Nottinghamshire Major County Award (by M. H. A.).

WILLIAM RAMSAY AND RALPH FORSTER LABORATORIES,
UNIVERSITY COLLEGE, LONDON, W.C.1. [*Received, July 1st,* 1958.]

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79. *Peroxides of Elements other than Carbon. Part IV.*[1] *The Autoxidation of Tri-*sec.*-butylboron to* sec.*-Butyldi-*(sec.*-butylperoxy)boron.*

By ALWYN G. DAVIES and D. G. HARE.

Tri-*sec.*-butylboron in dilute solution reacts readily with oxygen, giving *sec.*-butyldi-(*sec.*-butylperoxy)boron, $Bu^sB(O{\cdot}OBu^s)_2$, which has been isolated.

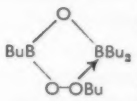
WE have shown [1] that the autoxidation of a mixed *iso*- and *tert.*-butylboron gave a similarly isomerically mixed diperoxide of the structure $BuB(O{\cdot}OBu)_2$. For further investigations it was desirable to obtain a product of unambiguous structure. The autoxidation of tri-*sec.*-butylboron, which does not isomerise,[2] has therefore been investigated.

In dilute solution in ether or nitromethane the alkyl absorbed 2 mol. of oxygen, giving a product containing approximately 2 mol. of peroxide, and from the oxidation in ether, *sec.*-butyldi-(*sec.*-butylperoxy)boron, $Bu^sB(O{\cdot}OBu^s)_2$, was isolated as a colourless oil. It was readily hydrolysed, and *sec.*-butyl hydroperoxide, *sec.*-butyl alcohol, and a trace of butan-2-one were identified in the vapour-phase chromatogram of the products. The hydroperoxide is stable under the isolation procedure; hence the small amount of ketone is probably formed by a base-catalysed carbonyl-forming elimination of the alkylperoxyboron compound,[3] where p_π–p_π overlap from oxygen to boron assists heterolysis of the O–O bond (cf. the heterolysis of the O–O bond in 2-phenyl-2-propylperoxyboron compounds [4]):

The *sec.*-butyl alcohol probably arises from the nucleophilic migration of the *sec.*-butyl group from boron to oxygen, as described in Part III.[1] The loss in peroxide which is observed when *sec.*-butyldi-(*sec.*-butylperoxy)boron in ether is treated with tertiary amines probably follows principally this second type of mechanism. The reactivity of different bases is in the order pyridine < 2 : 6-lutidine < triethylamine, and in the presence of a large excess of pyridine the reaction appears to be of first order with respect to boron peroxide.

[1] Part III, Abraham and Davies, preceding paper.
[2] Hennion, McCusker, Ashby, and Rutkowski, *J. Amer. Chem. Soc.*, 1957, **79**, 5190.
[3] Kornblum and de la Mare, *ibid.*, 1951, **73**, 880.
[4] Davies and Moodie, *J.*, 1958, 2372.

In aqueous suspension, tri-*sec.*-butylboron absorbed 1·52 mol. of oxygen, giving a product containing 0·98 mol. of peroxide, and probably consisting of the hydrolysis products of $Bu^sB(OBu^s)O{\cdot}OBu^s$. In pyridine solution the alkyl reacted relatively slowly, absorbing 1·33 mol. of oxygen, but giving a virtually non-peroxidic product; benzylamine completely inhibited the oxidation. This is consistent with the mechanism for the autoxidation suggested in Part III.[1]



sec.-Butylboronous anhydride in ether absorbed only 1 mol. of oxygen, giving a monoperoxy-compound; in water 1·70 mol. were absorbed, producing 1·22 mol. of peroxide. A possible interpretation of this is that under anhydrous conditions the monoperoxide (inset) is intramolecularly associated, thereby inhibiting autoxidation at the second Bu^s_2B group.

Experimental

The general methods for the preparation of capsules, the autoxidations, and the analyses are described in Part III.[1]

Tri-sec.-*butylboron*.—The reaction between *sec.*-butylmagnesium chloride and boron trifluoride in ether gave tri-*sec.*-butylboron (40% yield), b. p. 80—81°/12 mm., which was sealed under nitrogen in capsules (Found: B, 5·99. Calc. for $C_{12}H_{27}B$: B, 5·90%).[2]

sec.-*Butylboronous Anhydride*.—The reaction of *sec.*-butylmagnesium bromide and *n*-butyl ethylene borate in ether at −70° gave the ethylene ester of *sec.*-butylboronous acid; this was hydrolysed to the acid and dehydrated by fractional distillation with toluene, giving sec.-*butylboronous anhydride*, b. p. 113°/4 mm. (Found: B, 8·35. $C_{16}H_{36}OB_2$ requires B, 8·15%).

sec.-*Butyl Hydroperoxide*.—The "inverse" oxidation of *sec.*-butylmagnesium chloride in dilute ethereal solution at −75° gave *sec.*-butyl hydroperoxide,[5] b. p .29°/6 mm., n_D^{25} 1·4046. The infrared spectrum was identical with that described by Williams and Mosher.[6] This material was used for comparative chromatography.

Autoxidation of sec.-*Butylboron Compounds*.—The results are shown in the Table.

Solvent	Volume (c.c.)	Boron alkyl (g.)	Time (min.)	O_2 absorbed (mol.)	Peroxide formed (mol.)
		Tri-sec.-*butylboron*			
Et_2O	50	0·1468	45	1·91	1·70
Et_2O	50	0·1310	330	*a*	1·90
H_2O	75	0·1765	10	1·52	0·98
$Me{\cdot}NO_2$	50	0·1951	60	1·90	1·82
C_5H_5N	50	0·1868	210	1·33	0·0
$Ph{\cdot}CH_2{\cdot}NH_2$	25	0·1896	180	0·0	0·0
		sec.-*Butylboronous anhydride*			
Et_2O	50	0·1758	120	0·99	0·90
H_2O	50	0·7776	10	1·70	1·22

[a] Oxygen was dispersed through a sintered-glass plate into the solution of the alkylboron. All the other experiments were carried out with the gas burette.

Isolation of sec.-*Butyldi*-(sec.-*butylperoxy*)*boron*.—A capsule of tri-*sec.*-butylboron (0·6936 g.) was broken in ether (200 c.c.) through which nitrogen was passed, to give a dilute solution of the alkyl before autoxidation commenced. Oxygen was then passed through the solution for 7 hr., giving a product containing 1·97 mol. of peroxide. Stringent precautions were taken throughout to exclude moisture. The resulting solution was filtered from broken glass in the dry box, and the ether removed under reduced pressure, leaving *sec.*-butyldi-(*sec.*-butylperoxy)-boron as a clear oil [Found: C, 57·2 (uncorr.); H, 10·7; B, 4·40; peroxidic O, 24·6. Calc. for $C_{12}H_{27}O_4B$: C, 58·5; H, 11·1; B, 4·40; peroxidic O, 26·0%]. The peroxide was unreactive towards hydrogen and Raney nickel in ether at room temperature and pressure, and was not reduced by lithium aluminium hydride.

Hydrolysis of sec.-*Butyldi*-(sec.-*butylperoxy*)*boron*.—The peroxyboron compound was isolated

[5] Walling and Buckler, *J. Amer. Chem. Soc.*, 1955, **77**, 6032.
[6] Williams and Mosher, *Analyt. Chem.*, 1955, **27**, 517.

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after autoxidation of the alkyl (0·6683 g.) as described above. The product was shaken with water (25 c.c.) for 2 hr.; 2N-sodium hydroxide (5 c.c.) was then added, and the solution shaken for 0·5 hr., then extracted with ether (3 × 20 c.c.). The extract was dried ($MgSO_4$), and the bulk of the ether removed. Vapour-phase chromatography of the product showed the presence of *sec.*-butyl hydroperoxide, *sec.*-butyl alcohol, and a trace of butan-2-one. The infrared spectrum showed a weak carbonyl-group absorption at 5·95 μ and a strong peak at 11·66 μ characteristic of the O–O stretching frequency of *sec.*-butyl hydroperoxide.

With respect to this and the preceding paper, we are indebted to Professors E. D. Hughes, F.R.S., and Sir Christopher Ingold, F.R.S., for their interest and encouragement, and to Mr. P. J. Chaffe for technical assistance. This work was carried out during the tenure of a D.S.I.R. Fellowship by D. G. H.

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80. *Synthetical Applications of Activated Metal Catalysts. Part VI.* Desulphurisations with Raney Cobalt.*

By G. M. Badger, N. Kowanko, and W. H. F. Sasse.

Raney cobalt has been used to desulphurise dibenzothiophen and a number of acylthiophens, thiophencarboxylic acids, thiazoles, and thioamides. In general it is less effective than Raney nickel, but some differences have been noted.

Raney nickel has been extensively used in the desulphurisation of organosulphur compounds,[1,2] but other related catalysts have not been systematically investigated. A less active catalyst might have some advantages, especially if it could effect desulphurisation without the complete reduction of all unsaturated groups. Raney cobalt is a weak hydrogenation catalyst,[3,4] and its activity has now been compared with that of nickel in desulphurisation. An example of such use of Raney cobalt has been reported.[4]

Desulphurisation of 2-acetylthiophen with W-7 Raney nickel gives [2,5] hexan-2-one, and a little dodecane-2 : 11-dione. Under similar conditions, 2-benzoylthiophen gave some 1 : 8-dibenzoyloctane in addition to the expected valerophenone, and various thiophencarboxylic acids likewise also gave small amounts of dimeric products.[2,5] 2-Acetylthiophen, 2-benzoylthiophen, 3-acetylthionaphthen, thiophen-2-carboxylic acid, γ-2-thienylbutyric acid, and β-2-thenoylpropionic acid have now been desulphurised with Raney cobalt. However, on the basis of the extent of desulphurisation under similar conditions, W-7 Raney cobalt is much less effective than W-7 Raney nickel; in the desulphurisation of 3-acetylthionaphthen, for example, Raney cobalt was about one-tenth as active as Raney nickel.[5] Again small yields of dimer were generally obtained in addition to the expected monomeric products; but the ratio of dimer to monomer was not identical with that observed in experiments with Raney nickel. The desulphurisation of 2-benzoylthiophen with W-7 Raney cobalt, for example, gave no dibenzoyloctane, and with " Aller " Raney cobalt the ratio of dibenzoyloctane to valerophenone was 1 : 7·3. With W-7 Raney nickel, however, the ratio was 1 : 18·6, that is less than half the number of dimerisations for the number of molecules attacked. However, with γ-2-thienylbutyric acid, and in

* Part V, *J.*, 1957, 4417.

[1] Mozingo, Wolf, Harris, and Folkers, *J. Amer. Chem. Soc.*, 1943, **65**, 1013; Venkataraman, *J. Indian Chem. Soc.*, 1958, **35**, 1.
[2] Badger, Rodda, and Sasse, *J.*, 1954, 4162.
[3] Reeve and Christian, *J. Amer. Chem. Soc.*, 1956, **78**, 860; Ried and Schiller, *Chem. Ber.*, 1953, **86**, 730.
[4] Aller, *J. Appl. Chem.*, 1957, **7**, 130; 1958, **8**, 163.
[5] Badger and Sasse, *J.*, 1957, 3862.

agreement with the results obtained with nickel,[7] the proportion of dimer increased with the concentration of the reaction mixture. Such a result is, of course, expected if the dimer results from a recombination of free radicals.

Desulphurisations with Raney cobalt without simultaneous reduction of unsaturated groups could not be achieved. In the desulphurisation of β-2-thenoylpropionic acid there was some simultaneous reduction of the keto-group, for 4-hydroxyoctanolactone and 4 : 13-dihydroxyhexadecanedioic dilactone were obtained in addition to 4-oxo-octanoic acid and 4 : 13-dioxohexadecanedioic acid. Moreover, in the desulphurisation of 3-acetylthionaphthen 3-phenylbut-3-en-2-one could not be detected although this material was specially searched for, by using infrared spectroscopy.

The effect of W-7 Raney cobalt on thiazoles was similar to that of a rather weak nickel catalyst.[6] Some deamination of 2-amino-4-phenylthiazole occurred, and acetophenone was isolated. The thiol group of 2-mercaptobenzothiazole was removed, but no product resulting from the desulphurisation of the benzothiazole ring system could be detected.

Dibenzothiophen was also desulphurised by W-7 Raney cobalt, but here again the catalyst was less effective than nickel.[5] This experiment was carried out in ethanol as solvent, and a small amount of acetaldehyde was detected. However, the dehydrogenation was slower than with Raney nickel, and only after prolonged heating was sufficient aldehyde formed to permit identification.

The desulphurisation of phenanthridinethione offers a useful route to phenanthridine.[7] With active Raney nickel catalysts, however, the reaction is complicated by reduction to dihydrophenanthridine, necessitating a final dehydrogenation. With W-7 Raney cobalt, however, the desulphurisation smoothly gives phenanthridine in high yield. 2-Mercaptoquinoline with Raney cobalt gives quinoline, 2 : 2′-diquinolyl, and 2 : 2′-diquinolyl sulphide, together with a cobalt complex. Acridinethione was very resistant to desulphurisation by Raney cobalt, but some acridine and 9 : 9′-diacridyl were isolated. Imidazolidinethione did not yield imidazolidine, but gave ethylenediamine, presumably by hydrolysis of the parent base. Some *NN*-diformylethylenediamine was also isolated. It seems likely that the formylation of the ethylenediamine results from the action of the cobalt on the methanol solvent. In this respect Raney cobalt differs from Raney nickel, which does not formylate primary amines in methanol.[8]

2 : 2′-Dipyridyl could not be isolated following the refluxing of pyridine with either W-7 Raney cobalt or with a " degassed " cobalt. This behaviour is in marked contrast to that with Raney nickel.[9] Pyridine can therefore be used as a solvent for desulphurisations with Raney cobalt.

Experimental

Preparation of Raney Cobalt.—W-7 Raney cobalt was prepared from cobalt–aluminium alloy (30% Co, 70% Al; Lights) by the same method as for W-7 Raney nickel.[10] The more active " Aller " Raney cobalt was prepared at 15—20°.

Desulphurisation of 2-Acetylthiophen.—(i) A mixture of 2-acetylthiophen (30 g.), W-7 Raney cobalt catalyst (prepared from 125 g. of cobalt–aluminium alloy), and methanol (to 200 c.c.) was refluxed for 5 hr. The filtrate and methanol extracts of the catalyst were combined, methanol removed, and the residue distilled; three fractions were collected: (*a*) hexan-2-one, b. p. 60°/30 mm. (2·77 g.), identified as the dinitrophenylhydrazone; (*b*) 2-acetylthiophen, b. p. 102°/20 mm. (26·3 g.), identified as the dinitrophenylhydrazone; and (*c*) an oil, b. p. 80—90°/0·5 mm. (0·5 g.). Redistillation of fraction (*c*) and recrystallisation from light petroleum (b. p. <40°) gave dodecane-2 : 11-dione (10 mg.), m. p. and mixed m. p. 54—56°.

(ii) A mixture of 2-acetylthiophen (60 g.), W-7 Raney cobalt (from 250 g. of alloy), and methanol (to 250 c.c.) was refluxed for 24 hr. Distillation gave the following fractions: (*a*) a non-ketonic forerun, b. p. 100°/22 mm. (1·0 g.); (*b*) 2-acetylthiophen, b. p. 104—105°/22 mm.

[6] Badger and Kowanko, *J.*, 1957, 1652.
[7] Taylor and Martin, *J. Amer. Chem. Soc.*, 1952, **74**, 6295.
[8] Ainsworth, *J. Amer. Chem. Soc.*, 1956, **78**, 1635.
[9] Badger and Sasse, *J.*, 1956, 616.
[10] Billica and Adkins, *Org. Synth.*, 1949, **29**, 24.

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(50·75 g.); (*c*) an oil, b. p. 90—120°/0·03 mm. (0·996 g.); and (*d*) a small amount of solid removed from the neck of the flask. Fraction (*c*) was extracted seven times with light petroleum (b. p. <40°). Purification of the extracts by chromatography on alumina, and recrystallisation of the product from light petroleum gave dodecane-2 : 11-dione, plates, m. p. and mixed m. p. 54—56° (identity confirmed by infrared spectra). The petroleum-insoluble portion was identical with fraction (*d*) (by infrared spectra). Recrystallisation from benzene–light petroleum gave a *compound* as needles (30 mg.), m. p. 88·5—89° (Found: C, 58·1; H, 4·75; S, 24·3; O, 12·4%), whose spectrum in carbon tetrachloride (sodium chloride prism) showed a carbonyl band at 5·94 μ (suggesting a CO·C:C system), and a CH_2 absorption at 6·99 μ, but had little similarity to that of diacetyldithienyl.

Desulphurisation of 2-Benzoylthiophen.—(i) 2-Benzoylthiophen (30 g.), W-7 Raney cobalt (from 125 g. of alloy), and methanol (to 200 c.c.) were refluxed for 5 hr. Distillation of the product gave: (*a*) *n*-valerophenone, b. p. 80°/0·05 mm. (1·83 g.), identified as the dinitrophenylhydrazone; (*b*) 2-benzoylthiophen, b. p. 100—102°/0·05 mm. (24·75 g.); and (*c*) a residue from which 1 : 8-dibenzoyloctane could not be obtained.

(ii) In this experiment desulphurisation was effected as above except that Aller Raney cobalt was used. Distillation of the product gave (*a*) *n*-valerophenone, b. p. 80—100°/0·04 mm. (2·2 g.); (*b*) 2-benzoylthiophen, b. p. 110—120°/0·04 mm. (25·5 g.); and (*c*) a residue (0·5 g.), 1 : 8-dibenzoyloctane (30 mg., from ethanol), m. p. and mixed m. p. 92—93°.

Desulphurisation of 3-Acetylthionaphthen.—3-Acetylthionaphthen (30 g.), W-7 Raney cobalt (from 125 g. of alloy), and methanol (to 200 c.c.) were refluxed for 5 hr. Distillation gave: (*a*) a mixture (4·44 g.) from which 3-phenylbutan-2-one (1·4 g.; b. p. 110—112°/24 mm.; identified as the 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 171—172°) and 3-acetylthionaphthen (3·04 g.) were obtained; (*b*) 3-acetylthionaphthen, b. p. 96—102°/0·1 mm. (24·16 g.); and (*c*) a small intractable residue.

Desulphurisations of Acidic Derivatives of Thiophen.—(i) A stirred mixture of thiophen-2-carboxylic acid (5 g.), W-7 Raney cobalt (from 65 g. alloy), and 10% aqueous sodium carbonate (to 100 c.c.) was heated at 80—90° for 2 hr. The catalyst was removed and washed with hot sodium carbonate solution, and the aqueous solutions acidified. The precipitate of thiophen-2-carboxylic acid (3·75 g.) was removed and the liquors extracted with ether to give valeric acid (isolated as the *p*-bromobenzyl*iso*thiuronium salt, m. p. and mixed m. p. 162°; 3·3 g. equivalent to 0·97 g. of acid).

(ii) γ-2-Thienylbutyric acid (8·0 g.) was heated (steam-bath) and stirred with W-7 Raney cobalt (from 125 g. of alloy) in 10% aqueous sodium carbonate (to 900 c.c.) for 1·75 hr. Distillation of the acidic product gave: (*a*) *n*-octanoic acid, b. p. 72—73°/0·05 mm. (2·57 g.); (*b*) γ-2-thienylbutyric acid, b. p. 104°/0·05 mm. (4·90 g.), and (*c*) a residue (0·2 g.), which gave impure hexadecane-1 : 16-dicarboxylic acid (*ca.* 8 mg.), identified by its infrared spectrum.

(iii) γ-2-Thienylbutyric acid (30 g.), W-7 Raney cobalt (from 250 g. of alloy), and 10% aqueous sodium carbonate (300 c.c.) were heated for 5 hr. Distillation gave (*a*) a forerun (mainly octanoic acid), b. p. 60—80°/0·1 mm. (1·68 g.); (*b*) *n*-octanoic acid, b. p. 80°/0·1 mm. (6·25 g.); (*c*) γ-2-thienylbutyric acid, b. p. 115°/0·1 mm. (18·9 g.), and (*d*) a residue (1·2 g.). The residue (*d*) was extracted with sodium carbonate (charcoal), and the extract acidified. Recrystallisation from ether and then from concentrated nitric acid yielded hexadecane-1 : 16-dicarboxylic acid, m. p. and mixed m. p. 123—124°.

(iv) A stirred mixture of β-2-thenoylpropionic acid (7 g.), W-7 Raney cobalt (from 250 g. of alloy), and aqueous sodium carbonate (to 300 c.c.) was heated (steam-bath) for 5 hr. The catalyst was extracted with sodium carbonate, and the combined filtrates were acidified. On cooling, 4 : 13-dioxohexadecanedioic acid (0·27 g.), m. p. and mixed m. p. 152—153°, separated. Concentration of the mother liquors and cooling gave β-2-thenoylpropionic acid (1·415 g.), and the liquors were then extracted with ether, the ether evaporated, and the product distilled. Four fractions were collected: (*a*) 4-hydroxyoctanolactone, b. p. 114—118°/22 mm. (0·89 g.), n 1·4456 (lit. n_D^{19} 1·4451); (*b*) b. p. 152—166°/22 mm. (0·62 g.); (*c*) b. p. 180°/22 mm. (0·54 g.); and (*d*) a residue (0·5 g.). Recrystallisation of fractions (*b*) and (*c*) gave 4-oxo-octanoic acid, m. p. and mixed m. p. 50—52°. The residue was separated into an acidic and a neutral fraction. Repeated recrystallisation of the latter from benzene–light petroleum gave impure 4 : 13-dihydroxyhexadecane-1 : 16-dioic dilactone, m. p. 76—78° (3·7 mg.), identified by its infrared spectrum.

Desulphurisation of Thiazoles.—(i) A mixture of 2-amino-4-phenylthiazole (5 g.), W-7 Raney

cobalt (from 65 g. of alloy), and methanol (250 c.c.) was refluxed in a slow stream of nitrogen for 4 hr. The exit gases were passed into dilute hydrochloric acid (later evaporation of which gave ammonium chloride, 0·15 g.). The mixture furnished 2-amino-4-phenylthiazole (4·4 g.) and acetophenone (0·55 g.), identified and weighed as the dinitrophenylhydrazone.

(ii) 2-Mercaptobenzothiazole (10 g.) and W-7 Raney cobalt (from 65 g. of alloy) in methanol (250 c.c.) were refluxed for 4·5 hr. The catalyst was removed and well washed with boiling methanol, and the combined filtrates were acidified with dilute hydrochloric acid (100 c.c.), and distilled from the steam-bath. On cooling 2-mercaptobenzothiazole (3·0 g.) was deposited, and the liquors were treated with toluene-*p*-sulphonyl chloride (9·0 g.) and aqueous alkali. Steam distillation gave benzothiazole (2·74 g.), but amines could not be detected. A similar attempt to desulphurise benzothiazole (10 g.) gave unchanged material (6·08 g.) and a tar from which amines could not be obtained.

Desulphurisation of Dibenzothiophen.—A mixture of dibenzothiophen (5 g.), W-7 Raney cobalt (from 40 g. of alloy), and ethanol (200 c.c.) was refluxed for 14 hr. (A very faint reaction for acetaldehyde was obtained by passing a stream of nitrogen through the flask into a dimedone solution.) The filtrate was evaporated and the residue extracted with benzene (a little insoluble material being discarded), the benzene evaporated, and the product recrystallised from ethanol. The first crop on chromatography gave dibenzothiophen (1·8 g.), m. p. and mixed m. p. 98—99°, identified by formation of the picrate, m. p. and mixed m. p. 123—124°. The liquors were evaporated and the residue recrystallised from benzene–light petroleum (b. p. 40—60°) to give diphenyl (1·2 g.), m. p. and mixed m. p. 69—70°, also identified by formation of 4 : 4′-dibromodiphenyl, m. p. and mixed m. p. 169°.

Desulphurisation of Thioamides.—(i) A mixture of phenanthridinethione (1 g.), dimethylformamide (10 c.c.), ethanol (10 c.c.), and W-7 Raney cobalt (from 10 g. of alloy) was refluxed for 1·5 hr. The catalyst was removed from the hot solution and well washed with hot solvent, and the combined filtrates were evaporated under reduced pressure. After recrystallisation from acetone–water the crude phenanthridine (0·61 g., 72%) had m. p. 105—106°. Similar desulphurisation in pyridine gave less-pure phenanthridine.

(ii) A mixture of 2-mercaptoquinoline (3 g.), W-7 Raney cobalt (from 30 g. of alloy) and methanol (60 c.c.) was refluxed for 5 hr., a brown solid separating. The solid was washed well with boiling methanol, and the combined filtrates were evaporated to give 2 : 2′-diquinolyl (0·026 g.), m. p. and mixed m. p. 193—194°, and quinoline [isolated as the picrate (4·10 g.), m. p. and mixed m. p. 203°]. The mixed catalyst and brown solid were continuously extracted with hot dimethylformamide for 12 hr. Concentration to 10 c.c. gave *tris-(2-mercaptoquinoline)cobalt* (?) (0·455 g.), which formed shining black needles (from dimethylformamide) (Found: C, 60·3; H, 3·4; N, 7·4; S, 18·0; Co, 11·8. $C_{27}H_{4}N_{3}S_{3}Co$ requires C, 60·1; H, 3·4; N, 7·8; S, 17·8; Co, 10·9%). The dimethylformamide extracts after removal of the complex were diluted to 100 c.c. with water. The resulting solid was dried and chromatographed in benzene on alumina to give 2 : 2′-diquinolyl (0·295 g.), m. p. and mixed m. p. 193° (also red complex with Cu^{+}), and *di-2-quinolyl sulphide* (0·045 g.), which [from light petroleum (b. p. 100—120°)] had m. p. 188° (Found: C, 75·3; H, 4·4; N, 9·25; S, 11·1. $C_{18}H_{12}N_{2}S$ requires C, 75·0; H, 4·2; N, 9·7; S, 11·1%). Its m. p. was not depressed by admixture with a specimen prepared by fusing 2-chloroquinoline and sodium sulphide for 20 hr.

The complex was not affected by dilute hydrochloric acid. It was heated withc oncentrated hydrochloric acid at 140—160°, and the mixture poured into concentrated sodium hydroxide. Ether extraction gave 2-mercaptoquinoline (identified by paper chromatography) and diquinolyl sulphide (identified by paper chromatography and by its isolation as the picrate, m. p. and mixed m. p. 197°).

(iii) A mixture of acridinethione (3 g.), dimethylformamide (30 c.c.), ethanol (30 c.c.), and W-7 Raney cobalt (from 30 g. of alloy) was refluxed for 13 hr. The catalyst was separated, washed with hot dimethylformamide and with boiling ethanol, the combined filtrates evaporated, and the residue extracted with boiling 0·5N-sodium hydroxide (2 × 250 c.c.). The extracts on cooling and saturation with carbon dioxide gave acridinethione (0·92 g.). The alkali-insoluble portion was continuously extracted with light petroleum (b. p. 65—69°) for 2 hr. to give acridine [identified as the picrate (0·10 g.), m. p. and mixed m. p. 261—262°]. The petroleum-insoluble fraction (0·85 g.) was chromatographed in chlorobenzene on alumina to give 9 : 9′-diacridyl (0·43 g.), m. p. and mixed m. p. 393°. The chlorobenzene-insoluble fraction was not identified.

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(iv) A mixture of imidazolidinethione (10 g.), W-7 Raney cobalt (from 125 g. of alloy), and methanol (to 250 c.c.) was refluxed for 5 hr. The catalyst was washed with hot methanol, and the combined filtrates were concentrated to 75 c.c. Cooling gave imidazolidinethione (3·02 g.; m. p. and mixed m. p. 197—198°). Evaporation of the filtrate and distillation gave ethylenediamine [identified as the picrate (6·0 g.), m. p. and mixed m. p. 231—233°]. The residue (b. p. 100°/760 mm.) was treated with a little methanol and gave imidazolidinethione (1·61 g.) and a yellow, viscous oil (3·28 g.), b. p. 190°/0·01 mm., which partly solidified. Trituration with ethanol, and recrystallisation from ethanol and from ethyl acetate gave NN-*diformylethylenediamine* (2·68 g.), m. p. 109—110° not depressed by admixture with a specimen prepared by formylation of ethylenediamine (Found: C, 41·7; H, 7·1; N, 23·9; O, 27·5. $C_4H_8O_2N_2$ requires C, 41·4; H, 6·9; N, 24·1; O, 27·6%).

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81. *The Reaction between Diphenylamine and Malonic Esters.*

By R. E. BOWMAN, A. CAMPBELL, and (MISS) E. M. TANNER.

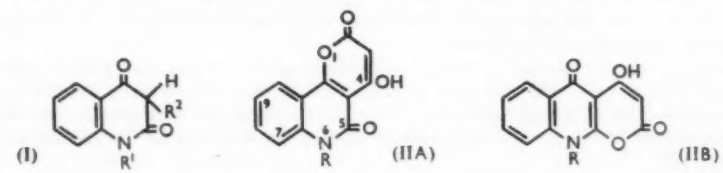
Diphenylamine with two mols. of malonic ester gives a product now shown to be the tricyclic amide (IIA; R = Ph); reaction with monoalkylmalonic esters, however, gave the expected 1 : 2 : 3 : 4-tetrahydro-2 : 4-dioxoquinolines (I).

BAUMGARTEN and RIEDEL [1] reported that diphenylamine condenses with boiling diethyl malonate with evolution of ethanol to give a high-melting solid formulated by them as 1 : 2 : 3 : 4-tetrahydro-2 : 4-dioxo-1-phenylquinoline (I; $R^1 = Ph$; $R^2 = H$). In our hands this reaction gave a product (II) of very similar physical properties to that obtained by these authors, but elemental analyses and molecular-weight determinations were consistent only with the formula $C_{18}H_{11}O_4N$, suggesting that, in fact, the base had reacted with two mols. of ester in the following manner:

$$Ph_2NH + 2CH_2(CO_2Et)_2 \longrightarrow C_{18}H_{11}O_4N + 4EtOH$$

A similar product was obtained from *N*-methylaniline.

On general considerations the structures (IIA or IIB; R = Me or Ph) appeared most likely to represent these compounds and evidence is adduced to support this conclusion.

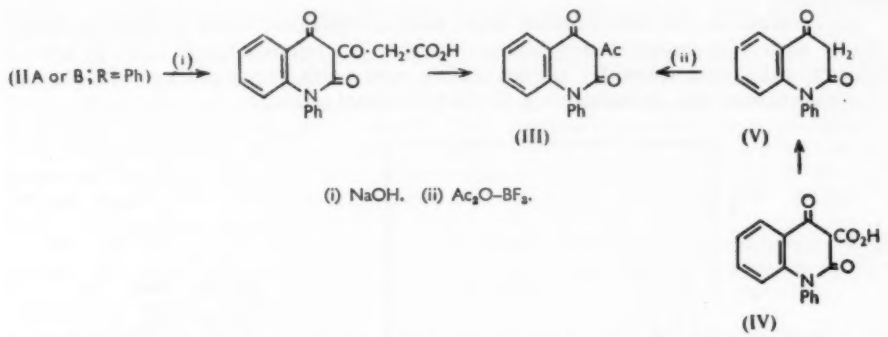


(I) (IIA) (IIB)

The infrared absorption spectrum of (II) showed strong bands at 1747, 1686, and 1572 cm.$^{-1}$ (in chloroform) consistent with the presence of a lactone carbonyl, cyclic amide carbonyl, and enolisable diketone system, respectively. The presence of the last group was confirmed by potentiometric titration (pK_a 8·64 in 85% dimethylformamide), and 1·2 active hydrogens were found by the Zerewitinov reaction. When heated with aqueous sodium hydroxide, the compound (II) was hydrolysed with concomitant loss of carbon dioxide to a compound $C_{17}H_{13}O_3N$ (III) in which the enolisable diketone system was still

[1] Baumgarten and Riedel, *Ber.*, 1942, **75**, *B*, 984.

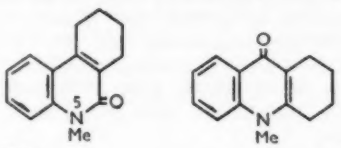
present (pK_a 9·26, and strong band at 1550 cm.$^{-1}$) but in which the ester group was no longer present as indicated by disappearance of the lactone-carbonyl band. Oxidation of this diketone with aqueous potassium permanganate gave a monocarboxylic acid



$C_{16}H_{11}O_4N$ (IV) which lost carbon dioxide at its melting point to give 1 : 2 : 3 : 4-tetrahydro-2 : 4-dioxo-1-phenylquinoline (V), identical in all respects with an authentic specimen prepared from acetic anhydride and diphenylamine.[2] These reactions, outlined above, are consistent with the formulation of the starting material as either (IIA) or (IIB).

Confirmatory evidence for the structure of the diketo-amide (III) was obtained by its resynthesis from (V) and acetic anhydride in the presence of boron trifluoride, a method which appears to be specific for the *C*-acylation of diketones.[3] Attempts to differentiate between the alternatives (IIA and IIB) by ozonolysis in acetic acid or carbon tetrachloride proved unfruitful, the sole product being the monocarboxylic acid (IV), due presumably to the enolisation of the β-diketone system in solution; a decision was therefore sought from spectral evidence.

The infrared spectra of α-quinolones and other six-membered heterocyclic amides are reported[4-6] to show strong carbonyl absorption bands in the 1680—1650 cm.$^{-1}$ region whereas γ-quinolones absorb strongly in the 1630—1620 cm.$^{-1}$ region. These differences also held in two model compounds containing a third ring, *e.g.*, (VI) and (VII), which had carbonyl bands at 1650 cm.$^{-1}$ and 1626 cm.$^{-1}$, respectively. It therefore appears that



(VI) (VII)

the 1686 cm.$^{-1}$ band in the spectrum of (II) favours an α- rather than a γ-quinolone structure. Furthermore, in the ultraviolet region, α-quinolones show a strong absorption peak at 320 mμ whereas γ-quinolones have a characteristic bifurcated band in the 320—360 mμ region,[5,6,8,9] the latter characteristic being found in the spectrum of (VII).

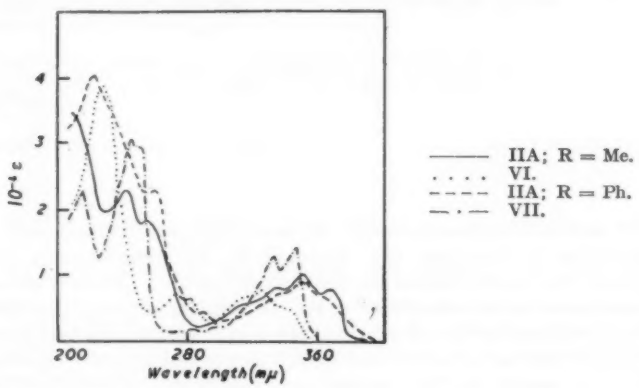
When allowance is made for the extra chromophore in (IIA) or (IIB) the ultraviolet

[2] B.P. 623,323.
[3] Rogers and Herchel Smith, *J.*, 1955, 341.
[4] Witcop, Patrick, and Rosenblum, *J. Amer. Chem. Soc.*, 1951, **73**, 2641.
[5] Grundon, McCorkindale, and Roger, *J.*, 1955, 4284.
[6] Edwards and Singh, *Canad. J. Chem.*, 1954, **32**, 687.
[7] Reed, *J.*, 1944, 425.
[8] Ewing and Steck, *J. Amer. Chem. Soc.*, 1946, **68**, 2181.
[9] Steck, Ewing, and Nachod, *ibid.*, 1949, **71**, 238.

XUM

absorption curve of (II) closely resembles those of α-quinolones and (VI) (Figure). Spectral evidence therefore fully supports the formulation of Baumgarten and Riedel's compound as (IIA) and formulæ of the derivatives described by them should be modified accordingly.

In contrast to the unsubstituted ester, monoalkylmalonic esters reacted equimolecularly with *N*-monosubstituted anilines to give 1 : 3-disubstituted 1 : 2 : 3 : 4-tetrahydro-2 : 4-dioxoquinolines (I); a series of these compounds, prepared for general pharmacological examination, is described in the Experimental section.



Experimental

Light petroleum refers to material of b. p. 40—60°. Infrared spectra are reported only for the 1750—1480 cm.$^{-1}$ region and, unless specified to the contrary, were obtained on "Nujol" mulls.

5 : 6-*Dihydro*-4-*hydroxy*-2 : 5-*dioxo*-6-*phenyl*-2H-*pyrano*[3,2-c]*quinoline* (IIA; R = Ph).—Ethyl malonate (400 g.) and diphenylamine (169 g.) were heated for 6 hr. during which ethanol (152 ml.) was collected by distillation through a short Vigreux column. The cooled (100°) mixture was stirred into methanol (1 l.) and the orange crystals (189 g., 62%) were collected and well rinsed with methanol. Many crystallisations from xylene and dioxan were required to give the *lactone* as colourless needles, m. p. 296—297° [Found: C, 70·7; H, 3·7; N, 4·6%; *M* (isothermal distillation in dimethylformamide), 284, 295. $C_{18}H_{11}O_4N$ requires C, 70·8; H, 3·6; N, 4·6%; *M*, 305]; pK_a 8·64 (in 85% dimethylformamide); $\lambda_{max.}$ (in ethanol) 220, 258, 289, 338 sh., 350, 362 sh. mμ (ε 40,200, 23,300, 4500, 7700, 8900, 7100, respectively); $\nu_{max.}$ 1751, 1691 s, 1666, 1622 w, 1579, 1563, 1506 s, 1439 (Nujol mull), and 1747 s, 1686, 1627 w, 1607 w, 1572 s cm.$^{-1}$ (chloroform).

5 : 6-*Dihydro*-4-*hydroxy*-6-*methyl*-2 : 5-*dioxo*-2H-*pyrano*[3,2-c]*quinoline* (IIA; R = Me).—Interaction of methylaniline and ethyl malonate under the same conditions as above furnished the lactone (99 g.; 41%) as a light brown powder. Crystallisation from dioxan and xylene gave the pure *product* as needles, m. p. 253—254° (Found: C, 64·0; H, 3·6; N, 5·6. $C_{13}H_9O_4N$ requires C, 64·2; H, 3·7; N, 5·8%); pK_a 8·30 (in 85% dimethylformamide); $\lambda_{max.}$ (in ethanol) 242, 254, 335 sh, 350, 366 mμ (ε 23,300, 18,500, 8000, 10,000, 8100); $\nu_{max.}$ 1750 s, 1683, 1626 w, 1587, 1554, 1511 w (Nujol mull), and 1747, 1692, 1626 w, 1583, 1558 cm.$^{-1}$ (chloroform).

Alkaline Hydrolysis of the Lactone (IIA; R = Ph).—A suspension of the lactone (27 g.) in 2N-sodium hydroxide (110 ml.) was refluxed for 2 hr. The resulting solution was cooled and acidified with 2N-hydrochloric acid to give the product as a voluminous white solid. Two crystallisations from methanol gave 3-*acetyl*-1 : 2 : 3 : 4-*tetrahydro*-2 : 4-*dioxo*-1-*phenylquinoline* (III) (21·9 g., 86%) as microneedles, m. p. 234° (Found: C, 72·9; H, 4·6; N, 5·1. $C_{17}H_{13}ON$ requires C, 73·1; H, 4·7; N, 5·0%); pK_a 9·26 (in 85% dimethylformamide); $\nu_{max.}$ 1657 s, 1550 s, 1487 sh. cm.$^{-1}$.

A solution of boron trifluoride (4 g.) in acetic acid (10 ml.) was added to a suspension of

1 : 2 : 3 : 4-tetrahydro-2 : 4-dioxo-1-phenylquinoline [2] (5 g.) in acetic anhydride (50 ml.); heat was evolved and the solid dissolved. After 20 min. the mixture was poured into water (200 ml.) containing sodium acetate (10 g.), and the crude product collected. Crystallisation from methanol gave 3-acetyl-1 : 2 : 3 : 4-tetrahydro-2 : 4-dioxo-1-phenylquinoline (1·9 g.; 31%), m. p. 233—234° undepressed by admixture with an equal weight of the material (III) obtained as above.

Permanganate Oxidation of the Quinoline (III).—Saturated aqueous potassium permanganate was added with stirring to a solution of the quinoline (III) (5 g.) in 50% aqueous acetone (200 ml.) until a permanent pink colour was observed. After removal of manganese dioxide, the filtrate was acidified and the precipitate collected. Two crystallisations from methanol furnished 1 : 2 : 3 : 4-tetrahydro-2 : 4-dioxo-1-phenylquinoline-3-carboxylic acid (IV) (1·2 g.) as pale yellow prisms, m. p. 187—189° (effervescence) with resolidification and melting at 295—298° (Found: C, 68·1; H, 4·0; N, 4·8%; equiv., 280. $C_{16}H_{11}O_4N$ requires C, 68·3; H, 3·9; N, 5·0%; equiv., 281); $\nu_{max.}$ 1687 s, 1622 s, 1598 w, 1574, and 1495 cm.$^{-1}$.

This acid (0·5 g.) was heated at 200° until effervescence ceased. Crystallisation of the residue from methanol gave 1 : 2 : 3 : 4-tetrahydro-2 : 4-dioxo-1-phenylquinoline as needles, m. p. 297—298° (decomp.) undepressed by admixture with an authentic specimen [2]; $\nu_{max.}$ 1629 s, 1586, 1540 s, 1497 s cm.$^{-1}$.

Ozonolysis of the Lactone (IIA ; R = Ph).—A stream of ozone was passed through a suspension of finely powdered lactone (IIA; R = Ph) (1 g.) in acetic acid (25 ml.) for 3 hr. until a clear yellow solution was obtained. Zinc dust (3 g.) was then added with stirring and after 1 hr., the excess was filtered off. Dilution of the filtrate with water and crystallisation from aqueous acetic acid gave 1 : 2 : 3 : 4-tetrahydro-2 : 4-dioxo-1-phenylquinoline-3-carboxylic acid identical in every respect with the material obtained previously.

7 : 8 : 9 : 10-*Tetrahydro-5-methylphenanthridone* (VI).—A solution of 7 : 8 : 9 : 10-tetrahydrophenanthridone [10] (0·5 g.) in acetone (20 ml.) containing anhydrous potassium carbonate (1 g.) and methyl iodide (2 g.) was refluxed for 2 hr. and then filtered. Evaporation of the filtrate yielded an oil which slowly crystallised. Crystallisation from light petroleum gave the *product* (0·3 g.) as leaflets, m. p. 63—64° (Found: C, 77·4; H, 7·4; N, 6·8. $C_{13}H_{15}O_4N$ requires C, 77·6; H, 7·5; N, 7·0%); $\nu_{max.}$ 1650 s, 1594 s, 1572 sh, 1503 sh (Nujol mull.), and 1653 s and 1608 cm.$^{-1}$ (carbon tetrachloride).

1 : 2 : 3 : 4-*Tetrahydro-10-methylacridone* (VII).—This material was prepared according to Reed's method.[7] It had infrared max. 1626, 1598, 1576 s, 1544 s (Nujol mull.), and 1626, 1607 s, 1579, and 1554 s cm.$^{-1}$ (chloroform).

1 : 3-*Dialkyl*-1 : 2 : 3 : 4-*tetrahydro*-2 : 4-*dioxoquinolines*.—A mixture of the *N*-alkylaniline (1 mol.) and monoalkylmalonic ester (1·3 mol.) was heated at the boiling point, ethanol of reaction being removed by fractionation through a Vigreux column. At the completion of the reaction, the mixture was cooled and the resulting solid crystallised from the appropriate solvent. In this manner the 1 : 3-dialkyl-1 : 2 : 3 : 4-tetrahydro-2 : 4-dioxoquinolines (I) recorded in the table were prepared

			Yield		Found (%)			Required (%)		
R^1	R^3	M. p.	(%)	Formula	C	H	N	C	H	N
Me	Ph	213—214° [1]	67	$C_{16}H_{13}O_2N$	76·4	5·1	5·5	76·5	5·2	5·6
Me	Bu	114—115 [3]	48	$C_{14}H_{17}O_2N$	72·5	7·2	5·1	72·7	7·4	6·1
CH_2·CH:CH_2	H	234—235 [3]	16·5	$C_{12}H_{11}O_2N$	71·7	5·3	6·9	71·6	5·5	7·0
CH_2·CH:CH_2	Bu	110—111 [3]	80	$C_{16}H_{19}O_2N$	74·6	7·3	5·5	74·7	7·4	5·4
CH_2·CH:CH_2	Ph	166—167 [1]	35	$C_{18}H_{15}O_2N$	77·8	5·3	5·0	78·0	5·5	5·1
Ph	Bu	206—207 [4]	52	$C_{19}H_{19}O_2N$	77·9	6·3	4·8	77·8	6·5	4·8

[1] Needles from methanol. [3] Prisms from chloroform–light petroleum. [3] Plates from chloroform–light petroleum. [4] Needles from chloroform–light petroleum.

RESEARCH DEPT., PARKE, DAVIS & CO. LTD.,
STAINES ROAD, HOUNSLOW, MIDDX.

[*Received, October 9th*, 1958.]

[10] Blount, Perkin, and Plant, *J.*, 1929, 1986.

XUM

82. *Organic Nitrates. Part II.** 9-*Fluorenyl Nitrate.*

By G. W. H. Cheeseman.

The nitrate is converted into fluorenone by a variety of basic reagents and thus shows a marked tendency to undergo carbonyl elimination rather than to react by alkyl–oxygen fission.

9-Fluorenyl nitrate was prepared by reaction of equimolecular amounts of 9-chlorofluorene and silver nitrate in methyl cyanide. This reaction was considerably slower than that of 9-bromofluorene,[1,2] but the chloro-compound was very readily prepared from fluoren-9-ol.[3] 9-Fluorenyl nitrate was comparatively stable at room temperature, whereas diphenylmethyl nitrate decomposed within a few hours at this temperature.[4] One batch of the nitrate did, however, decompose, with the evolution of brown fumes, after storage at room temperature for several months. Freeman [2] obtained fluoren-9-ol and fluorenone by thermal decomposition of the nitrate in chlorobenzene; fluorenone was also obtained when the nitrate was heated at 140° for 1 hr.

The reaction of 9-fluorenyl nitrate and aniline in the absence of solvent gave 9-anilinofluorene and aniline nitrate. When the reactants were dissolved in ether and the solution set aside at room temperature for 48 hr., the water-soluble nitrite formed indicated that a small percentage of α-hydrogen elimination had occurred, and unchanged nitrate was recovered from the ether-soluble products. When the nitrate was treated in methyl cyanide solution with benzylamine or morpholine, the yield of water-soluble nitrite was practically quantitative. Fluorenone was isolated from the ether-soluble products of the benzylamine reaction, and in the morpholine experiment the yield was nearly quantitative. A quantitative yield of fluorenone was also obtained on reaction of the nitrate with pyridine in methyl cyanide. Similarly fluorenone was formed exclusively when the nitrate was treated with methanolic potassium hydroxide.[2] From this work it was clear that 9-fluorenyl nitrate underwent carbonyl-elimination much more readily than diphenylmethyl nitrate. Baker and Heggs [5] studied the effects of structural changes on the carbonyl-elimination reactions of aralkyl nitrates, showing that carbonyl elimination was favoured by conjugation of a 1-phenyl substitutent with the forming double bond, also by factors which increase the strength of the nitric ester as a pseudo-acid. In the transition state for the formation of benzophenone both phenyl groups tend to conjugate with the forming carbonyl bond, but in the transition state for the formation of fluorenone a high degree of conjugation is possible between the forming double bond and the two coplanar *ortho*-linked phenyl groups. The pseudo-acidity of fluorene derivatives is well known. This is due to the peculiar stability of the *cyclo*pentadienyl-type anions resulting from the separation of a proton from position 9.[6]

When fluorenyl nitrate was heated with excess of acetamide, *N*-9-fluorenylacetamide was formed. Fluorenyl nitrate, however, failed to react with ethanol, thiophenol, sodium toluene-*p*-sulphinate, or 1 : 3 : 5-trimethoxybenzene under the mild conditions which led to reaction in the case of diphenylmethyl nitrate.[4] Thus, whereas diphenylmethyl nitrate underwent rapid solvolysis in ethanol at 20°, fluorenyl nitrate was recovered essentially unchanged after 72 hr. in solution in ethanol at room temperature. Rapid solvolysis did, however, occur at the boiling point of the solvent. Similarly, although diphenylmethyl

* Part I, *J.*, 1957, 115. A preliminary account of some of the present work has appeared in *Chem. and Ind.*, 1956, 1390.

[1] Eaborn and Shaw, *J.*, 1955, 1420.
[2] Freeman, *J. Org. Chem.*, 1956, **21**, 471.
[3] Arcus and Mesley, *J.*, 1953, 180.
[4] Cheeseman, *J.*, 1957, 115.
[5] Baker and Heggs, *J.*, 1955, 616.
[6] Wilson Baker, "Perspectives in Organic Chemistry," Interscience Publ. Ltd., London, 1956, p. 37.

chloride is rapidly solvolysed in aqueous ethanol at 25°,[7] 9-chlorofluorene may be crystallised from this solvent. Fluorenyl nitrate did not react with thiophenol in methyl cyanide at room temperature. After 22 hr. at 56°, a mixture was obtained which on oxidation yielded some 9-fluorenyl phenyl sulphone. When a solution of the nitrate in thiophenol was set aside at room temperature, a vigorous reaction eventually took place. The products were separated chromatographically and diphenyl disulphide and fluorenone were isolated. Fluorenyl nitrate failed to react with sodium toluene-*p*-sulphinate in acetic acid or in boiling benzene; with ethanol as solvent a mixture of sulphone and 9-ethoxyfluorene was obtained. The decreased reactivity of fluorenyl nitrate compared with that of diphenylmethyl nitrate in these reactions, which are diagnostic of esters undergoing unimolecular alkyl–oxygen heterolysis,[8] indicated that the fluorenyl cation was the less readily formed. Conductivity measurements in sulphur dioxide at 0° show that 9-chloro-9-phenylfluorene has less tendency to ionise than has triphenylmethyl chloride.[9] It is suggested that the chloride shares in some of the resonance stabilisation of the 9-phenylfluorenyl anion whereas the cation does not. Conversely any factors which stabilise the cation would be expected to increase the degree of ionisation.

Freeman [2] observed that when 9-fluorenyl nitrate was dissolved in 95% sulphuric acid a deep blue-green colour appeared, and that fluoren-9-ol was formed when the solution was poured into water. When a drop of 72% perchloric acid was added to a solution of the nitrate in methyl cyanide an intense colour appeared. Anisole was added to this solution, but no 9-*p*-methoxyphenylfluorene was isolated from the mixture after 24 hr. at room temperature. The perchloric acid-catalysed reaction of fluoren-9-ol with anisole and phenol in nitromethane at 100° gave 9-*p*-methoxyphenylfluorene and 9-*p*-hydroxyphenylfluorene, respectively.

Experimental

Ethereal solutions were dried by azeotropic distillation with benzene. Nitrite was estimated colorimetrically.[10]

9-Fluorenyl Nitrate.—A mixture of 9-chlorofluorene (40·0 g., 0·20 mole) and silver nitrate (34·0 g., 0·20 mole) in methyl cyanide (150 ml.) was heated at 53° for 7 hr., then left overnight at room temperature. Silver chloride was filtered off and the filtrate evaporated in a vacuum. Extraction of the residue with light petroleum (b. p. 40—60°; 750 ml.) gave 9-fluorenyl nitrate as needles (27·3 g.), m. p. 86—89°. A further crop (9·5 g.), m. p. 80—85°, was obtained by concentration of the mother-liquor. The analytical specimen was crystallised from light petroleum (b. p. 40—60°; 15 parts) and had m. p. 88—89° (Found: C, 69·1; H, 4·0; N, 6·0. Calc. for $C_{13}H_9O_3N$: C, 68·7; H, 4·0; N, 6·2%). Eaborn and Shaw [1] give m. p. 89°. Extraction with glacial acetic acid of the light petroleum-insoluble material gave colourless needles of di-(9-fluorenyl) ether, m. p. 229—231°. The m. p. was raised to 231—232° by further crystallisation from glacial acetic acid (50 parts) (Found: C, 90·0; H, 5·5. Calc. for $C_{26}H_{18}O$: C, 90·1; H, 5·2%). Kleigl [11] gives m. p. 228°.

Decomposition of 9-Fluorenyl Nitrate.—The nitrate (1·15 g.) was heated at 140—150° for 1 hr. Water and ether were added, and the organic layer was separated, washed free from acid, dried, and evaporated. Crystallisation of the residue from 96% ethanol gave fluorenone (0·35 g.), m. p. and mixed m. p. 80—83°.

Reaction of 9-Fluorenyl Nitrate with Amines.—(a) *With aniline.* Heat was evolved when the nitrate (1·15 g.) and aniline (1·0 ml.) were mixed. After 2 hr., benzene was added and the crystalline precipitate of aniline nitrate (0·6 g.), m. p. 199—201° (decomp.), filtered off. The filtrate was evaporated in a vacuum and the residue (1·55 g.) shaken in ether with excess of 2N-hydrochloric acid. The hydrochloride which separated was filtered off and was

[7] Ward, *J.*, 1927, 2285.
[8] Davies and Kenyon, *Quart. Rev.*, 1955, **9**, 203.
[9] Leffler, "The Reactive Intermediates of Organic Chemistry," Interscience Publ. Ltd., London, 1956, p. 79.
[10] Barnes and Folkard, *Analyst*, 1951, **76**, 55.
[11] Kleigl, *Ber.*, 1910, **43**, 2488.

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decomposed by treatment with ether and 2N-sodium hydroxide. The dried ethereal layer was evaporated in a vacuum. Crystallisation of the residual 9-anilinofluorene (0·92 g., 71%; m. p. 122—124°) from 96% ethanol (20 parts) gave needles, m. p. 123—124° (undepressed on admixture with an authentic sample [12]).

A mixture of the nitrate (3·4 g., 0·015 mole) and aniline (2·8 g.) in ether (30 ml.) was set aside for 2 days at room temperature, then poured into water. The ethereal layer was separated, and washed with water until the washings no longer gave a positive nitrite reaction, and then with 2N-hydrochloric acid. 9-Fluorenyl nitrate was recovered from the dried ethereal layer. The combined aqueous washings contained 0·00056 mole (4%) of nitrite.

(b) *With benzylamine.* When 9-fluorenyl nitrate (5·6 g., 0·025 mole) in methyl cyanide (20 ml.) was added to a solution of benzylamine (5·35 g., 0·05 mole) in methyl cyanide (10 ml.), heat was evolved. After 18 hr., water and ether were added, and the organic layer was separated and washed with water until the washings no longer gave a positive nitrite reaction. An unidentified yellow solid (0·2 g.), m. p. (mainly) 216—226°, separated slowly from the organic layer. This was collected and its m. p. was raised to 227—228° by two crystallisations from aqueous pyridine (Found: C, 88·8; H, 5·4; N, 5·5%). Evaporation of the dried filtrate and crystallisation of the residue from 96% ethanol gave fluorenone, m. p. and mixed m. p. 82—83° (oxime, m. p. and mixed m. p. 194—195°). The combined aqueous washings contained 0·023 mole (92%) of nitrite.

(c) *With morpholine.* When 9-fluorenyl nitrate (2·3 g., 0·01 mole) was added to a solution of morpholine (1·8 g.) in methyl cyanide (5 ml.) a vigorous reaction occurred. After 18 hr. the mixture was poured into water and ether, and the organic layer was separated and washed with water until the washings no longer gave a positive nitrite reaction. Evaporation of the dried ethereal layer gave fluorenone (1·76 g., 98%), m. p. and mixed m. p. 80—84°. The combined aqueous washings contained 0·010 mole (100%) of nitrite.

(d) *With pyridine.* Pyridine (1·6 ml.) was added to a solution of 9-fluorenyl nitrate (2·3 g.) in methyl cyanide (5 ml.). The mixture was then set aside at room temperature overnight. On dilution with water, nitrous fumes were evolved. The precipitate of fluorenone (1·8 g., 100%) had m. p. and mixed m. p. 82—84°.

Reaction of 9-Fluorenyl Nitrate with Acetamide.—A mixture of the nitrate (2·3 g.) and acetamide (2·4 g.) was heated at 100° for 30 min. Water was added and the residual oil solidified by trituration with 96% ethanol. The crystalline product (1·15 g., 52%), m. p. 249—255° (decomp.), gave colourless needles of *N*-9-fluorenylacetamide of unchanged m. p., on crystallisation from benzene (200 parts) or 96% ethanol (150 parts) (Found: C, 80·4; H, 6·0; N, 6·5. Calc. for $C_{15}H_{13}ON$: C, 80·7; H, 5·9; N, 6·3%). The amide is reported [13, 14] to have m. p. 246° and 262°.

Reaction of 9-Fluorenyl Nitrate with Ethanol.—The nitrate (1·15 g.) was heated under reflux with ethanol (10 ml.) for 30 min. and then cooled. Addition of water precipitated an oil which gradually solidified. The crude product (0·95 g., 90%) had m. p. *ca.* 40—50°. Successive crystallisations from aqueous ethanol gave colourless crystals of 9-ethoxyfluorene, m. p. 53—54° (Found: C, 85·7; H, 6·95. Calc. for $C_{15}H_{14}O$: C, 85·7; H, 6·7%). Loevenich, Becker, and Schröder [15] give m. p. 54°.

Reaction of 9-Fluorenyl Nitrate with Thiophenol.—(*a*) A mixture of the nitrate (1·15 g.) and thiophenol (1·15 ml.) was set aside at room temperature. After some hours a vigorous reaction occurred. The product was isolated in ether and, after evaporation of solvent, the residue (1·85 g.) was dissolved in 1 : 10 benzene–light petroleum (b. p. 40—60°). The solution was filtered through a column of aluminium oxide (100 g.; Spence, type H, mesh 100—200), and the chromatogram developed with benzene–light petroleum (b. p. 40—60°) mixtures. A fraction (0·82 g.), m. p. 48—56°, eluted with 1 : 10 benzene–light petroleum, gave colourless needles of diphenyl disulphide (0·72 g.), m. p. and mixed m. p. 60—61° (from 96% ethanol). A fraction (0·20 g.), m. p. 69—73°, eluted with 1 : 1 benzene–light petroleum, gave fluorenone, m. p. and mixed m. p. 82—83° [from *cyclo*hexane–light petroleum (b. p. 40—60°)].

(*b*) A mixture of the nitrate (2·3 g.) and thiophenol (2·3 ml.) in methyl cyanide (5 ml.) was heated at 56° for 22 hr. After cooling, the crystalline precipitate (0·43 g.), m. p. 209—212°

[12] Courtot and Petitcolas, *Compt. rend.*, 1925, **180**, 297.
[13] Langecker, *J. prakt. Chem.*, 1932, **132**, 145.
[14] Goldschmidt, *Annalen*, 1927, **456**, 152.
[15] Loevenich, Becker, and Schröder, *J. prakt. Chem.*, 1930, **127**, 248.

was filtered off. Crystallisation from acetic acid gave needles of di-(9-fluorenyl) ether, m. p. 225—227°. The original filtrate was diluted with water and ether, and the organic layer was separated, washed with water, dried, and evaporated. Crystallisation of the residue from benzene (5 ml.) and light petroleum (b. p. 40—60°; 5 ml.) gave impure fluoren-9-ol (0·45 g.), m. p. and mixed m. p. 139—142°. The mother-liquor was evaporated and the residue oxidised at room temperature with hydrogen peroxide (30% w/w; 5 ml.) in glacial acetic acid (50 ml.). After 18 hr., water was added and the crude product filtered off. Repeated crystallisations from 96% ethanol gave *9-fluorenyl phenyl sulphone* as needles, m. p. 181—183° (Found: C, 74·0; H, 4·7; S, 11·0. $C_{19}H_{14}O_2S$ requires C, 74·5; H, 4·6; S, 10·5%).

*Reaction of 9-Fluorenyl Nitrate with Sodium Toluene-*p*-sulphinate.*—The nitrate (1·15 g.) was heated with sodium toluene-*p*-sulphinate (1·8 g.) in ethanol (20 ml.), under reflux for 45 min. After cooling, the precipitate was filtered off and extracted with water. The resulting 9-fluorenyl *p*-tolyl sulphone (0·5 g., 31%) had m. p. 225—227°. The m. p. was unchanged by crystallisation from butan-1-ol (20 parts) and was undepressed on admixture with an authentic sample.[16] Addition of water to the ethanolic mother-liquor precipitated 9-ethoxyfluorene (0·15 g.), m. p. 52—53·5°.

The nitrate failed to react with a suspension of powdered sodium toluene-*p*-sulphinate in boiling benzene.

9-p-*Hydroxyphenylfluorene.*—72% Perchloric acid (3 drops) was added to a solution of fluoren-9-ol (3·64 g.) and phenol (9·4 g.) in nitromethane (10 ml.). The mixture was kept at 100° for 3 hr., then cooled, and poured into water and ether. The organic layer was separated, washed free from acid, dried, and evaporated. Excess of phenol was removed in steam. Three crystallisations of the residue (4·6 g.), m. p. (mainly) 123—163°, from benzene, gave 9-*p*-hydroxyphenylfluorene as colourless needles, m. p. 182—183° (decomp.) (Found: C, 88·6; H, 5·7. Calc. for $C_{19}H_{14}O$: C, 88·35; H, 5·5%). Bistrzycki and von Weber [17] give m. p. 178—179° (decomp.).

9-p-*Methoxyphenylfluorene.*—72% Perchloric acid (3 drops) was added to a solution of fluoren-9-ol (3·64 g.) in anisole (12 ml.) and nitromethane (12 ml.). The mixture was kept at 100° for 3 hr., then cooled, and poured into water and ether. The organic layer was separated, washed free from acid, and dried. Solvent and excess of anisole were removed at 100°/20 mm. Crystallisation of the residue from ethanol gave colourless needles of 9-*p*-methoxyphenylfluorene (1·75 g., 32%), m. p. 117—120°. The m. p. was raised to 122—123° by further crystallisation from ethanol (10 parts) and light petroleum (b. p. 60—80°; 5 parts) (Found: C, 88·1; H, 6·2. Calc. for $C_{20}H_{16}O$: C, 88·2; H, 5·9%). Bistrzycki and von Weber [17] give m. p. 121—122°.

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[*Received, August 25th,* 1958.]

[16] Ingold and Jessop, *J.*, 1930, 708.
[17] Bistrzycki and von Weber, *Ber.*, 1910, **43**, 2496.

XUM

83. *Organic Nitrates. Part III.* Triphenylmethyl Nitrate and 9-Phenyl-9-fluorenyl Nitrate.*

By G. W. H. Cheeseman.

Triphenylmethyl nitrate is extremely unstable and decomposes on attempted isolation. 9-Phenyl-9-fluorenyl nitrate is more stable, but is also hydrolysed in contact with air. The alkyl–oxygen bond in these compounds undergoes ready fission in a variety of reactions.

Experiments with diphenylmethyl nitrate [1a] suggested that triphenylmethyl nitrate would have versatile alkylating properties. In the case of the triphenylmethyl compound the possibility of concurrent α-hydrogen elimination reactions was structurally excluded.

Triphenylmethyl nitrate was prepared in ethereal solution from triphenylmethyl chloride and excess of powdered silver nitrate. Evaporation of the ethereal solution gave the solid nitrate which was converted into triphenylmethanol on short exposure to air.[1b] When the nitrate was heated with acetamide, *N*-triphenylmethylacetamide was formed in excellent yield. Merrow and Boschan [2] similarly alkylated hydrazine by reaction with the nitrate in ether. Interaction of ethereal solutions of triphenylmethyl nitrate and phenylmagnesium bromide gave some tetraphenylmethane.

As triphenylmethyl perchlorate was known to alkylate suitably activated aromatic compounds,[3] it was of interest to attempt to carry out similar reactions with triphenylmethyl nitrate. When a solution of triphenylmethyl chloride in anisole was added to one of silver nitrate in methyl cyanide, the subsequent reaction gave silver chloride, *N*-triphenylmethylacetamide, and a mixture of *o*- and *p*-nitroanisole, and may be represented by the following overall equation:

$$Ph_3C{\cdot}Cl + PhOMe + AgNO_3 + MeCN \longrightarrow Me{\cdot}CO{\cdot}NH{\cdot}CPh_3 + MeO{\cdot}C_6H_4{\cdot}NO_2 + AgCl$$

Cristol and Leffler [4] have isolated a compound which they suggest may be the nitrate of the imidol form of *N*-triphenylmethylacetamide, from the reaction of a solution of triphenylmethyl chloride in methyl cyanide with one of silver nitrate in methyl cyanide:

$$Ph_3C{\cdot}Cl + AgNO_3 + MeCN \longrightarrow Me{\cdot}C(O{\cdot}NO_2){:}N{\cdot}CPh_3 + AgCl$$

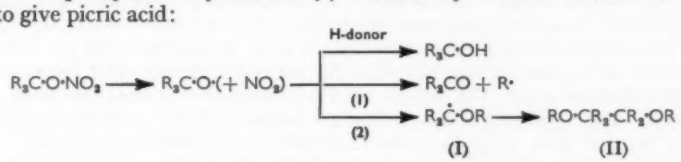
This substance was readily converted into *N*-triphenylmethylacetamide on crystallisation from commercial acetone or 96% ethanol. When *N*-triphenylmethylacetamide was formed in the system, triphenylmethyl chloride–anisole–silver nitrate–methyl cyanide, the bulk of the amide (80% of the total yield) crystallised directly from the reaction mixture. This suggests that imidol nitrate–anisole interaction may give *N*-triphenylmethylacetamide and nitroanisole. The parallel reactions between triphenylmethyl chloride dissolved in anisole, and silver nitrate dissolved in ethyl cyanide, phenyl cyanide, benzyl cyanide, and vinyl cyanide (acrylonitrile) were carried out, and the corresponding *N*-triphenylmethylamides isolated. A solution of silver nitrate in methyl cyanide underwent reaction with a 1 : 3-dimethoxybenzene solution of triphenylmethyl chloride to give *N*-triphenylmethylacetamide and a mixture of dimethoxynitrobenzenes, and with an anisole solution of *p*-methoxytriphenylmethyl chloride to give *N*-*p*-methoxytriphenylmethylacetamide.

Triphenylmethyl nitrate was extremely sensitive to hydrolysis: thus hydrolysis of the nitrate occurred when solutions of the nitrate in ether,[1a] benzene, or carbon tetrachloride [4] were exposed to air. The nitrate decomposed when heated under reflux in benzene [2] or toluene solution, oxides of nitrogen being evolved and triphenylmethanol formed. The

* Part II, preceding paper.

[1] Cheeseman, (*a*) *J.*, 1957, 115; (*b*) *Chem. and Ind.*, 1954, 281.
[2] Merrow and Boschan, *J. Amer. Chem. Soc.*, 1954, **76**, 4622.
[3] Burton and Cheeseman, *J.*, 1953, 832.
[4] Cristol and Leffler, *J. Amer. Chem. Soc.*, 1954, **76**, 4468.

decomposition of the nitrate presumably gives nitrogen dioxide and triphenylmethoxy-radicals which abstract hydrogen from a suitable donor to give triphenylmethanol. Cristol and Leffler [4] found that thermal decomposition of the nitrate in carbon tetrachloride or nitrobenzene gave triphenylmethanol, benzophenone, picric acid, and oxides of nitrogen. In order to explain the formation of benzophenone and picric acid they postulated β-cleavage of triphenylmethoxy-radicals (I) followed by a series of oxidation–reduction reactions to give picric acid:



Hawthorne [5] has prepared the more stable tri-*p*-nitrophenylmethyl nitrate and examined its thermal decomposition in chlorobenzene in the absence of air. This produced tri-*p*-nitrophenylmethanol, 4 : 4′-dinitrobenzophenone, 2 : 4-dinitrophenol, and the compound (II; R = *p*-$NO_2{\cdot}C_6H_4$), resulting from the Wieland rearrangement (2) of the tri-*p*-nitrophenylmethoxy-radical to the radical (I; R = *p*-$NO_2{\cdot}C_6H_4$), and subsequent dimerisation. An alternative path for the production of 4 : 4′-dinitrobenzophenone and 2 : 4-dinitrophenol involving the rearranged radical (I; R = *p*-$NO_2{\cdot}C_6H_4$) was also proposed.

In view of the difficulties in carrying out experiments with triphenylmethyl nitrate, 9-phenyl-9-fluorenyl nitrate was prepared. The structure of this tertiary nitrate was also such as to eliminate the possibility of both α- and β-hydrogen elimination. 9-Phenyl-9-fluorenyl nitrate was obtained by the action of excess of powdered silver nitrate on an ethereal solution of 9-chloro-9-phenylfluorene. The nitrate crystallised readily from ether–light petroleum mixtures and melted with decomposition at *ca.* 116—117°. The crystalline nitrate was hydrolysed (to 9-phenylfluoren-9-ol) on exposure to air, but less rapidly than triphenylmethyl nitrate. Heating the nitrate in an atmosphere of dry ammonia at 100° afforded di-(9-phenyl-9-fluorenyl) ether and 9-phenylfluoren-9-ol. Reaction of the nitrate with aniline and morpholine gave 9-anilino- and 9-morpholino-9-phenylfluorene, respectively. Treatment with excess of acetamide gave *N*-(9-phenyl-9-fluorenyl)acetamide; this compound was also obtained in high yield by heating a mixture of 9-phenylfluoren-9-ol and acetamide in the presence of a catalytic amount of concentrated sulphuric acid. The reaction of equimolecular amounts of the nitrate and toluene-*p*-sulphonamide in methyl cyanide gave a low yield of the expected sulphonamide. This was probably due to concurrent reaction of the nitrate with solvent, as a solution of the nitrate in methyl cyanide at room temperature soon became yellow and brown fumes were evolved. Addition of water precipitated high-melting solid of relatively high nitrogen content, indicating that nitration may have occurred. 9-Phenyl-9-fluorenyl nitrate underwent rapid solvolysis in methanol or ethanol at room temperature. Reaction with thiophenol, 1 : 3 : 5-trimethoxybenzene, and sodium toluene-*p*-sulphinate in ether at room temperature gave phenyl 9-phenyl-9-fluorenyl sulphide, 1 : 3 : 5-trimethoxy-2-(9-phenyl-9-fluorenyl)benzene, and 9-phenyl-9-fluorenyl *p*-tolyl sulphone, respectively. In these respects 9-phenyl-9-fluorenyl nitrate showed the typical reactivity of an ester undergoing unimolecular alkyl–oxygen heterolysis.[6]

Experimental

Ethereal solutions were dried by azeotropic distillation with benzene.

Reaction of Triphenylmethyl Nitrate with Acetamide.—Powdered silver nitrate (10 g.) was added to a solution of triphenylmethyl chloride (7·0 g.) in dry ether (50 ml.). The mixture was

[5] Hawthorne, *J. Amer. Chem. Soc.*, 1955, **77**, 5521.
[6] Davies and Kenyon, *Quart. Rev.*, 1955, **9**, 362.

XUM

heated under reflux for 1 hr., then filtered in a closed system. The residual silver chloride weighed 3·59 g. (100%) after being washed with water. Acetamide (5·9 g.) was added to the ethereal filtrate, solvent was removed, and the residue heated at 80—120° for 1 hr. The mixture was then cooled and extracted with water, and *N*-triphenylmethylacetamide (6·95 g., 92%), m. p. (mainly) 204—210°, filtered off. Crystallisation from benzene (11 parts) gave the pure amide, m. p. 211—213° (undepressed on admixture with an authentic sample [7]).

Reaction of Triphenylmethyl Nitrate with Phenylmagnesium Bromide.—A solution of triphenylmethyl nitrate (from triphenylmethyl chloride, 7·0 g.) in ether (50 ml.) was added dropwise to one of phenylmagnesium bromide (prepared from magnesium, 1·25 g.). The mixture, from which solid had separated, was heated under reflux for 15 min., then cooled and decomposed with 2N-sulphuric acid. The organic layer was separated, washed free from acid, dried, and evaporated. Ether (25 ml.) was added to the residue, and the solid filtered off. Crystallisation from benzene gave tetraphenylmethane (0·2 g.) as needles, m. p. 274—277°. The m. p. was raised to 278—280° by further crystallisation from benzene (30 parts) and sublimation at 220—230°/1 mm. (Found: C, 93·8; H, 6·2. Calc. for $C_{25}H_{20}$: C, 93·7; H, 6·3%). Ullmann and Münzhuber [8] give m. p. 282°.

Reaction in the System, Triphenylmethyl Chloride–Anisole–Silver Nitrate–Methyl Cyanide.—Triphenylmethyl chloride (13·9 g., 0·05 mole) in anisole (21·6 g., 0·20 mole) was added dropwise to a water-cooled solution of silver nitrate (8·5 g., 0·05 mole) in methyl cyanide (25 ml.), so that the temperature did not exceed 20°. The mixture was set aside at room temperature for 3 days, and the solid obtained by filtration was extracted with benzene (Soxhlet). The residual silver chloride weighed 7·0 g. (97%) and the extract yielded *N*-triphenylmethylacetamide (9·9 g.), m. p. 212—213°. The m. p. was unchanged by crystallisation from ethanol (20 parts) and was undepressed on admixture with an authentic sample [7] (Found: C, 84·0; H, 6·5; N, 4·7. Calc. for $C_{21}H_{19}ON$: C, 83·7; H, 6·35; N, 4·7%). The original filtrate was poured into water and ether, and the organic layer separated, washed free from acid, dried and evaporated. Solvent and excess of anisole were removed by heating to 80°/1·5 mm. Crystallisation of the residue from benzene gave *N*-triphenylmethylacetamide (2·6 g.), m. p. 211—212°. The total yield was thus 83%. The mother-liquor was evaporated in a vacuum; distillation of the residue at 0·8 mm. gave a nitroanisole fraction (6·0 g., 78%), b. p. 101—105°. The analytical specimen had b. p. 92—93°/0·7 mm., n_D^{17} 1·571 (Found: C, 55·9; H, 5·0; N, 8·7. Calc. for $C_7H_7O_3N$: C, 54·9; H, 4·6; N, 9·15%).

Reaction in the System, Triphenylmethyl Chloride–Anisole–Silver Nitrate–Ethyl Cyanide.—Triphenylmethyl chloride (13·9 g.) in anisole (21·6 g.) was caused to react similarly with a solution of silver nitrate (8·5 g.) in ethyl cyanide (25 ml.). After 7 days at room temperature, the mixture was filtered and the solid extracted with benzene (Soxhlet). The extract gave *N-triphenylmethylpropionamide* (7·0 g., 44%), m. p. 193—194°. The m. p. was unchanged by further crystallisation from benzene (10 parts) (Found: C, 84·1; H, 6·7; N, 4·1. $C_{22}H_{21}ON$ requires C, 83·8; H, 6·7; N, 4·4%). The original filtrate was poured into ether and water. Distillation of the washed and dried organic layer yielded a nitroanisole fraction (3·8 g., 50%), b. p. 105—108°/1·5 mm., n_D^{21} 1·568. The residue gave impure triphenylmethanol, m. p. (mainly) 142—149°, on crystallisation from benzene.

Reaction in the System, Triphenylmethyl Chloride–Anisole–Silver Nitrate–Phenyl Cyanide.—Triphenylmethyl chloride (6·95 g.) in anisole (10·8 g.) was caused to react similarly with a solution of silver nitrate (4·25 g.) in phenyl cyanide (10 ml.). After 7 days at room temperature, the mixture was filtered, and the filtrate poured into ether and water. The washed and dried organic layer yielded a nitroanisole fraction (2·5 g., 65%), b. p. 98—110°/1·5 mm., n_D^{19} 1·570, on distillation. Crystallisation of the residue from ethanol gave *N*-triphenylmethylbenzamide (4·9 g., 54%), m. p. 160—163°. The pure amide, m. p. 163—164°, was obtained by successive crystallisation from ethanol (5 parts) and benzene–light petroleum (b. p. 40—60°) (1 : 2; 6 parts) (Found: C, 86·0; H, 6·1; N, 3·7. Calc. for $C_{26}H_{21}ON$: C, 85·9; H, 5·8; N, 3·9%). The m. p.s recorded [9, 10] for this compound are 160—162° and 165·5°.

Reaction in the System, Triphenylmethyl Chloride–Anisole–Silver Nitrate–Benzyl Cyanide.—Triphenylmethyl chloride (6·95 g.) in anisole (10·8 g.) was caused to react similarly with

[7] Fosse, *Bull. Soc. chim. France*, 1931, **49**, 159.
[8] Ullmann and Münzhuber, *Ber.*, 1903, **36**, 409.
[9] Vosburgh, *J. Amer. Chem. Soc.*, 1916, **38**, 2087.
[10] Brander, *Rec. Trav. chim.*, 1918, **37**, 78.

a solution of silver nitrate (4·25 g.) in benzyl cyanide (10 g.). After 7 days at room temperature, the mixture was filtered and the solid extracted with benzene (Soxhlet). The extract yielded N-(*triphenylmethyl*)*phenylacetamide* (6·2 g., 66%), m. p. (mainly) 186—188°. Successive crystallisation from benzene (5 parts) and ethanol (20 parts) gave the pure amide, m. p. 191—192° (Found: C, 86·0; H, 6·1; N, 3·6. $C_{27}H_{23}ON$ requires C, 85·9; H, 6·1; N, 3·7%).

Reaction in the System, Triphenylmethyl Chloride–Anisole–Silver Nitrate–Acrylonitrile.—Triphenylmethyl chloride (6·95 g.) in anisole (10·8 g.) was caused to react similarly with a solution of silver nitrate (4·25 g.) in acrylonitrile (10 ml.). After 7 days at room temperature, the mixture was filtered and the filtrate poured into ether and water. The organic layer was separated, washed with water, dried, and heated to 100°/20 mm. Ether was added to the residual oil, and, after cooling, the solid (1·0 g.), m. p. 185—192°, filtered off. Crystallisation from ethanol gave N-*triphenylmethylacrylamide* (0·6 g., 8%), m. p. 203—205°. The m. p. was raised to 204—206° by further crystallisation from ethanol (25 parts) (Found: C, 84·2; H, 6·3; N, 4·7. $C_{22}H_{19}ON$ requires C, 84·3; H, 6·1; N, 4·5%).

*Reaction in the System, Triphenylmethyl Chloride–*1 : 3-*Dimethoxybenzene–Silver Nitrate–Methyl Cyanide.*—Triphenylmethyl chloride (6·95 g.) in 1 : 3-dimethoxybenzene (13·8 g.) was caused to react similarly with a solution of silver nitrate (4·25 g.) in methyl cyanide (25 ml.). The mixture was set aside at room temperature for 2 days and then filtered. The solid was extracted with chloroform (Soxhlet). Evaporation of the extract gave *N*-triphenylmethylacetamide (1·85 g.), m. p. 211—213°. The filtrate was distilled in steam and *ca.* 2 l. of distillate collected. Crystallisation of the non-volatile solid from ethanol gave *N*-triphenylmethylacetamide (1·75 g.), m. p. (mainly) 208—210°. The total yield was thus 48%. The distillate deposited needles (1·0 g.) on cooling, which after two crystallisations from ethanol (10 parts) gave slightly impure 2 : 4-dimethoxy-1-nitrobenzene, m. p. 69—71° (Found: C, 52·9; H, 4·9; N, 7·45. Calc. for $C_8H_9O_4N$: C, 52·4; H, 4·95; N, 7·65%). 2 : 4-Dimethoxy-1-nitrobenzene is reported to have m. p.s ranging from 73° to 76—77°.

Reaction in the System, p-*Methoxytriphenylmethyl Chloride–Anisole–Silver Nitrate–Methyl Cyanide.*—*p*-Methoxytriphenylmethyl chloride (6·17 g., 0·02 mole) in anisole (12·9 g., 0·12 mole) was caused to react similarly with a solution of silver nitrate (3·4 g., 0·02 mole) in methyl cyanide (50 ml.). After 4 days at room temperature, the mixture was filtered and the filtrate distilled in steam. The non-volatile material (6·4 g.) was extracted with ether and N-(*p-methoxytriphenylmethyl*)*acetamide* (2·7 g., 41%), m. p. (mainly) 173—177° filtered off in two crops. The m. p. was raised to 180—181° by crystallisation from aqueous acetone (Found: C, 79·4; H, 6·4. $C_{22}H_{21}O_2N$ requires C, 79·7; H, 6·4%). Treatment of the ethereal mother-liquor with acetyl chloride gave *p*-methoxytriphenylmethyl chloride, m. p. 118—122° (undepressed on admixture with an authentic sample [11]). Chloroform extraction of the steam distillate and distillation of the dried extracts gave a nitroanisole fraction (0·6 g.), b. p. (mainly) 134°/2·2 mm., n_D^{22} 1·565.

Reaction in the System, Triphenylmethyl Chloride–Silver Nitrate–Methyl Cyanide.—Triphenylmethyl chloride (6·95 g.) was added to a solution of silver nitrate (4·25 g.) in methyl cyanide (25 ml.). After 7 days at room temperature, the mixture was filtered and the filtrate poured into ether and water. The residual silver chloride weighed 3·5 g. (98%). The organic layer was separated, washed free from acid, dried, and evaporated. Treatment of the residue with ether (50 ml.) gave *N*-triphenylmethylacetamide (0·7 g.), m. p. (mainly) 198—209°. The m. p. was raised to 209—212° by crystallisation from benzene and was undepressed on admixture with an authentic sample. Concentration of the ethereal mother-liquor gave triphenylmethanol, m. p. and mixed m. p. 160—162·5°.

9-*Phenyl*-9-*fluorenyl Nitrate.*—Powdered silver nitrate (1·7 g., 0·01 mole) was added to a solution of 9-chloro-9-phenylfluorene [12] (2·8 g., 0·01 mole) in dry ether (25 ml.), and the mixture heated under reflux for 1 hr. Silver nitrate (1·7 g.) was then added and heating continued for 1 hr. Silver salts were filtered off; the residual silver chloride weighed 1·45 g. (100%) after being washed with water. The filtrate was evaporated in a vacuum and ether (15 ml.) added to the residue. Small amounts of insoluble matter were removed, and the filtrate was diluted with light petroleum (b. p. 40—60°; 15 ml.). On refrigeration, colourless crystals of 9-*phenyl*-9-*fluorenyl nitrate* separated; a sample heated from 90° had m. p. *ca.* 116—117° (decomp.)

[11] Burton and Cheeseman, *J.*, 1955, 3089.
[12] Hurd and Mold, *J. Org. Chem.*, 1948, **13**, 339.

XUM

(Found: C, 75·6; H, 4·3; N, 4·3. $C_{19}H_{13}O_3N$ requires C, 75·25; H, 4·3; N, 4·6%). Complete solvolysis showed 98% purity. The nitrate was stored at 0° in a desiccator (KOH). Complete solvolysis after 4 weeks showed 92% purity.

Decomposition of 9-Phenyl-9-fluorenyl Nitrate.—(a) *At room temperature.* The nitrate (1·05 g.) was left in a porcelain dish at room temperature for several days. 96% Ethanol (5 ml.) and water (1 ml.) were then added. After cooling, the crystalline precipitate of 9-phenylfluoren-9-ol (0·5 g.), m. p. 108—110° (undepressed on admixture with an authentic sample [13]), was filtered off.

(b) *In methyl cyanide.* A solution of the nitrate (0·91 g.) in methyl cyanide (10 ml.) became yellow at room temperature and nitrous fumes were evolved. After 18 hr., water was added, and the crystalline precipitate (0·7 g.), m. p. 219—222°, was filtered off. The m. p. was raised to 226—227° by successive crystallisation from ethanol (75 parts) and aqueous acetic acid (Found: C, 75·8; H, 5·1; N, 7·0%).

(c) *On heating in an atmosphere of ammonia.* A solution of the nitrate (from 9-chloro-9-phenylfluorene, 2·8 g.) in ether (25 ml.) was evaporated in a stream of dry ammonia. The residue was then heated cautiously in an atmosphere of ammonia to 100°, and kept at 100° for 1 hr. 2N-Hydrochloric acid and chloroform were added, and the organic layer was separated, washed free from acid, dried, and evaporated. Crystallisation of the residue from methanol (5 ml.) gave di-(9-phenyl-9-fluorenyl) ether (0·6 g.), m. p. (mainly) 210—220°. Successive crystallisation from ethanol (200 parts) and *cyclo*hexane (20 parts) furnished crystals, m. p. 237—239° (undepressed on admixture with an authentic sample [14]) (Found: C, 91·2; H, 5·6. Calc. for $C_{38}H_{26}O$: C, 91·2; H, 5·3%). The methanolic mother-liquor was evaporated and the residue extracted with light petroleum (b. p. 60—80°; 100 ml.). The extract slowly deposited crystals of 9-phenylfluoren-9-ol, m. p. 107—109°.

A sample of the nitrate heated at 120° for 30 min. decomposed to give an oil from which no crystalline material was isolated.

Reaction of 9-Phenyl-9-fluorenyl Nitrate with Aniline.—Aniline (1·86 ml.) was added to a solution of the nitrate (from 9-chloro-9-phenylfluorene, 2·8 g.) in ether (25 ml.). The mixture was left at room temperature overnight, then poured into water. The organic layer was separated, washed successively with water, 2N-sodium hydroxide, and water, dried, and evaporated. Methanol (10 ml.) was added to the residue, and the precipitate of 9-anilino-9-phenylfluorene (1·8 g., 54%), m. p. (mainly) 173—175°, filtered off. The m. p. was raised to 178—180° by two crystallisations from butan-1-ol (10 parts), and was undepressed on admixture with an authentic sample.[15]

Reaction of 9-Phenyl-9-fluorenyl Nitrate with Morpholine.—Morpholine (2 ml.) was added to a solution of the nitrate (from 9-chloro-9-phenylfluorene, 2·8 g.) in ether (25 ml.). The mixture was left at room temperature overnight and then solvent was removed. Water was added to the residue, and the product filtered off. Crystallisation from butan-1-ol gave *9-morpholino-9-phenylfluorene* (1·8 g., 55%), m. p. 228—230°. The m. p. was raised to 233—234° by crystallisation from either light petroleum (b. p. 80—100°; 60 parts) or butan-1-ol (20 parts) (Found: C, 84·0; H, 6·7; N, 4·3. $C_{23}H_{21}ON$ requires C, 84·4; H, 6·5; N, 4·3%).

In another experiment, a reaction mixture of similar composition was left at room temperature overnight and then poured into water. The organic layer was separated, washed with water, dried, and evaporated, and the residue dissolved in methanol (5 ml.). On dilution with a little water, an oil was precipitated which gradually solidified. After several crystallisations of the crude product (1·2 g.), m. p. (mainly) 77—87°, from 96% ethanol, 9-methoxy-9-phenylfluorene, m. p. 94—95°, was obtained (Found: C, 88·0; H, 6·2. Calc. for $C_{20}H_{16}O$: C, 88·2; H, 5·9%). Kleigl [15] gives m. p. 92·5—93°. The aqueous-methanolic mother-liquor yielded a fraction (0·3 g.) of m. p. (mainly) 210—225°. Crystallisation from light petroleum (b. p. 60—80°) gave 9-morpholino-9-phenylfluorene, m. p. 230—232°. Evaporation of the combined aqueous washings gave a crystalline residue, which yielded morpholine nitrate, m. p. 140—142° (undepressed on admixture with an authentic sample [16]), on recrystallisation from ethanol.

9-Morpholino-9-phenylfluorene was also obtained by heating a mixture of 9-chloro-9-phenylfluorene (2·8 g.) and morpholine (10 ml.) at 95° for 2 hr. Water was then added and the

[13] Ullmann and von Wurstemberger, *Ber.*, 1904, **37**, 73.
[14] Gomberg, *J. Amer. Chem. Soc.*, 1913, **35**, 200.
[15] Kleigl, *Ber.*, 1905, **38**, 284.

precipitate filtered off. Crystallisation from light petroleum (b. p. 80—100°) gave the pure morpholino-compound (2·6 g., 80%), m. p. 232—234°.

Reaction of 9-*Phenyl*-9-*fluorenyl Nitrate with Acetamide.*—Acetamide (3·0 g.) was added to a solution of the nitrate (from 9-chloro-9-phenylfluorene, 2·8 g.) in ether (25 ml.). Solvent was removed and the residue heated at 80—100° for 1 hr. The mixture was then extracted with water, and the product (3·0 g.), m. p. (mainly) 220—225°, filtered off. Crystallisation from benzene (50 parts) gave *N*-(9-phenyl-9-fluorenyl)acetamide (2·1 g., 70%), m. p. 228—230°. The m. p. was unchanged by further crystallisation from ethanol (40 parts) (Found: C, 84·1; H, 5·8; N, 4·4. Calc. for $C_{21}H_{17}ON$: C, 84·2; H, 5·7; N, 4·7%). Pinck and Hilbert [16] give m. p. 232°.

The amide was also obtained by heating 9-phenylfluoren-9-ol (3·0 g.), acetamide (3·0 g.) and concentrated sulphuric acid (5 drops) at 210—220° for 45 min. After cooling, the mixture was extracted with water, and the product (3·5 g.), m. p. (mainly) 223—227°, filtered off. Crystallisation from butan-1-ol (12 parts) gave the amide (2·8 g., 81%), m. p. 228—231°.

Reaction of 9-*Phenyl*-9-*fluorenyl Nitrate with Toluene*-p-*sulphonamide.*—A mixture of the nitrate (1·52 g.) and toluene-*p*-sulphonamide (0·85 g.) in methyl cyanide (10 ml.) was set aside at room temperature overnight. Water was added, and, after refrigeration, the precipitate filtered off and dissolved in hot 96% ethanol (40 ml.). The solution was allowed to cool to room temperature, then filtered. The filtrate deposited crystals of N-(9-*phenyl*-9-*fluorenyl*)-*toluene*-p-*sulphonamide* (0·25 g., 12%), m. p. (mainly) 188—192°. The m. p. was raised to 193—194° by two further crystallisations from 96% ethanol (100 parts) (Found: C, 75·9; H, 5·5; N, 3·2; S, 7·5. $C_{26}H_{21}O_2NS$ requires C, 75·6; H, 5·15; N, 3·4; S, 7·8%).

Reaction of 9-*Phenyl*-9-*fluorenyl Nitrate with Ethanol.*—A mixture of the nitrate (0·61 g.) and ethanol (10 ml.) was set aside at room temperature overnight. Water was then added and the precipitate of 9-ethoxy-9-phenylfluorene (0·56 g., 97%), m. p. (mainly) 113—114°, filtered off. Crystallisation from 96% ethanol (20 parts) gave the pure ethoxy-compound, m. p. 114—115° (undepressed on admixture with an authentic sample [15]) (Found: C, 88·2; H, 6·5. Calc. for $C_{21}H_{18}O$: C, 88·0; H, 6·3%).

Reaction of 9-*Phenyl*-9-*fluorenyl Nitrate with Thiophenol.*—Thiophenol (1·1 ml.) was added to a solution of the nitrate (from 9-chloro-9-phenylfluorene, 2·8 g.) in ether (25 ml.). After 18 hr., solvent was removed. The crystalline residue (2·2 g., 65%) had m. p. (mainly) 116—119°, after washing with a little ether. Crystallisation from 96% ethanol (25 parts) gave *phenyl* 9-*phenyl*-9-*fluorenyl sulphide*, m. p. 118—120° (Found: C, 85·2; H, 5·3; S, 9·1. $C_{25}H_{18}S$ requires C, 85·7; H, 5·2; S, 9·15%).

Reaction of 9-*Phenyl*-9-*fluorenyl Nitrate with* 1 : 3 : 5-*Trimethoxybenzene.*—1 : 3 : 5-Trimethoxybenzene (1·7 g.) was added to a solution of the nitrate (from 9-chloro-9-phenylfluorene, 2·8 g.) in ether (25 ml.). After 18 hr., the mixture was poured into excess of sodium hydrogen carbonate solution. The organic layer was separated, washed with water, dried, and evaporated. 96% Ethanol (10 ml.) was added to the residue, and the crystalline precipitate filtered off. Crystallisation from 96% ethanol gave 1 : 3 : 5-*trimethoxy*-2-(9-*phenyl*-9-*fluorenyl*)-*benzene* (2·4 g., 59%), m. p. 165—167°. The m. p. was unchanged by further crystallisation from 96% ethanol (50 parts) and light petroleum (b. p. 60—80°; 40 parts) (Found: C, 82·2; H, 6·1. $C_{28}H_{24}O_3$ requires C, 82·3; H, 5·9%).

The trimethoxy-compound was also prepared by adding 72% perchloric acid (2 drops) to a solution of 9-phenylfluoren-9-ol (2·6 g.) and 1 : 3 : 5-trimethoxybenzene (1·7 g.) in nitromethane (10 ml.). The mixture was left at room temperature overnight and then filtered. Crystallisation of the product from 96% ethanol gave 1 : 3 : 5-trimethoxy-2-(9-phenyl-9-fluorenyl)-benzene (3·2 g., 78%), m. p. 164—166°. This compound apparently crystallised in a low-melting form, m. p. 149—152°, from benzene–light petroleum (b. p. 40—60°) (1 : 1; 6 parts).

Reaction of 9-*Phenyl*-9-*fluorenyl Nitrate with Sodium Toluene*-p-*sulphinate.*—Powdered sodium toluene-*p*-sulphinate (2·7 g.) was added to a solution of the nitrate (from 9-chloro-9-phenylfluorene, 2·8 g.) in ether (25 ml.). The reaction mixture was heated under reflux for 1 hr., then left at room temperature for 3 days. Solvent was removed and water added to the residue. The sticky solid was filtered off and washed with ether. The ethereal layer was separated from the combined filtrate and washings, washed successively with water, sodium hydrogen carbonate solution, and water, dried, and evaporated. Methanol (5 ml.) was added to the residue and the solid filtered off. The total yield of 9-phenyl-9-fluorenyl *p*-tolyl sulphone

[16] Pinck and Hilbert, *J. Amer. Chem. Soc.*, 1937, **59**, 8.

XUM

was thus 0·70 g. (19%), m. p. (mainly) 209—210°. The m. p. was raised to 211—212° by crystallisation from ethanol (70 parts) and was undepressed on admixture with an authentic sample.[17] 9-Methoxy-9-phenylfluorene, m. p. 93—94°, was isolated from the methanolic mother-liquor, indicating that the nitrate had only partly reacted.

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[*Received, August 25th,* 1958.]

[17] Bassey, Buncel, and Davies, *J.*, 1955, 2550.

NOTES.

84. *Some Reactions of Xanthhydryl Chloride.*

By G. W. H. CHEESEMAN.

REPLACEMENT of chlorine occurred when xanthhydryl chloride [1] was treated with silver nitrate in ether at room temperature, and xanthone crystallised from the solution. At 0°, silver chloride was also formed, and evaporation of the resulting solution in air gave xanthone. As the chloride was at least partly converted into nitrate in these experiments, it seems likely that xanthhydryl nitrate very readily decomposes into xanthone. Xanthone was also isolated on reaction of the chloride and silver nitrate in methyl cyanide, together with some *N*-xanthhydrylacetamide. Kny-Jones and Ward [1] isolated xanthone, xanthen, and some xanthhydrol after the action of water on xanthhydryl chloride; in this case xanthone and xanthen were produced by the ready acid-catalysed dismutation of the xanthhydrol formed in the primary reaction. It has now been found that treatment of the chloride in ether at room temperature with morpholine, thiophenol, or 1 : 3 : 5-trimethoxybenzene gave 4-xanthhydrylmorpholine, phenyl xanthhydryl sulphide, and 1 : 3 : 5-trimethoxy-2-xanthhydrylbenzene, respectively. When ethereal solutions of the chloride and phenylmagnesium bromide were mixed and heated under reflux for 3 hr., 9-phenylxanthen was formed.

Experimental.—Xanthhydryl chloride was freshly prepared [1] and used without purification.

Reaction of xanthhydryl chloride with silver nitrate. (*a*) In ether. Powdered silver nitrate (8·5 g.) was added to a solution of xanthhydryl chloride (from xanthhydrol, 5·0 g.) in dry ether (50 ml.). The mixture was shaken for 4 hr. at room temperature and then filtered. The solid obtained by filtration was extracted with benzene (Soxhlet). The extract yielded xanthone (1·65 g.), m. p. and mixed m. p. 174—176°. The residual silver chloride weighed 2·65 g. after being washed with water. Acetamide (6·0 g.) was added to the original filtrate, solvent was removed, and the residue heated at 100° for 30 min. Successive extraction of the mixture with water and acetone (50 ml.) gave *N*-xanthhydrylacetamide (1·2 g.), m. p. 246—248°. The m. p. was unchanged by crystallisation from 96% ethanol and was undepressed on admixture with an authentic sample.[2]

When an ethereal solution of xanthhydryl chloride (from xanthhydrol, 5·0 g.) was stirred with powdered silver nitrate (8·5 g.) for 1 hr. at 0°, 1·25 g. of silver chloride were formed. The filtered solution was divided into two portions. One portion was allowed to evaporate at room temperature: crystallisation of the residue from 96% ethanol gave xanthone as needles, m. p. 168—174°. The remainder was stirred with powdered sodium toluene-*p*-sulphinate at room temperature for 1 hr., then set aside at room temperature overnight; the mixture was filtered and the solid obtained extracted with water; successive crystallisation from acetone (40 parts) and ethanol (100 parts) gave *p*-tolyl xanthhydryl sulphone, m. p. 213—214° (undepressed on admixture with an authentic sample [3]) (Found: C, 71·6; H, 5·1; S, 9·35. Calc. for $C_{20}H_{16}O_3S$: C, 71·4; H, 4·8; S, 9·5%).

[1] Kny-Jones and Ward, *J.*, 1930, 535.
[2] Vogel, "Practical Organic Chemistry," Longmans, Green & Co., London, 1948, p. 398.
[3] Balfe, Kenyon, and Thain, *J.*, 1952, 790.

(*b*) In methyl cyanide. Xanthhydryl chloride (from xanthhydrol, 6·0 g.) dissolved rapidly in a solution of silver nitrate (7·0 g.) in methyl cyanide (20 ml.). The mixture was set aside for 90 min. at room temperature and then filtered. The solid obtained was extracted with benzene (Soxhlet) and, on cooling, *N*-xanthhydrylacetamide (0·6 g.), m. p. 243—245°, separated from the extract. Concentration of the mother-liquor gave xanthone (1·15 g.), m. p. (mainly) 169—173°. The original filtrate was evaporated; decomposition occurred during the attempted crystallisation of the residue from light petroleum (b. p. 60—80°), and only xanthone (1·8 g.), m. p. (mainly) 169—173°, was isolated.

Reaction of xanthhydryl chloride with morpholine. Xanthhydryl chloride (from xanthhydrol, 2·0 g.) was caused to react with morpholine (3 ml.) in ether at room temperature. After 18 hr., solvent was removed, the residue extracted with water, and the product (2·2 g.) filtered off. Crystallisation from ethanol (15 parts) gave *4-xanthhydrylmorpholine* (1·4 g., 52%), m. p. 139—140° (Found: C, 76·6; H, 6·65; N, 5·3. $C_{17}H_{17}O_2N$ requires C, 76·4; H, 6·4; N, 5·2%).

Reaction of xanthhydryl chloride with thiophenol. Xanthhydryl chloride (from xanthhydrol, 2·85 g.) was caused to react similarly with thiophenol (2 ml.). After 18 hr., the mixture was poured into water and ether. The organic layer was separated, washed with water, dried, and evaporated. Light petroleum (b. p. 40—60°) was added to the residue, and, after cooling to 0°, the crystalline precipitate (2·8 g., 67%), m. p. 74—76°, filtered off. Crystallisation from 96% ethanol (6 parts) gave phenyl xanthhydryl sulphide, m. p. 78—79° (Found: C, 78·5; H, 5·0; S, 10·9. Calc. for $C_{19}H_{14}OS$: C, 78·6; H, 4·85; S, 11·0%). Sawicki and Oliverio [4] give m. p. 77—78°. The sulphide was converted into xanthone, m. p. 176—177°, on oxidation with hydrogen peroxide in glacial acetic acid.

Reaction of xanthhydryl chloride with 1 : 3 : 5-trimethoxybenzene. Xanthhydryl chloride (from xanthhydrol, 4·0 g.) was caused to react similarly with 1 : 3 : 5-trimethoxybenzene (3·4 g.). After 18 hr., the product (5·1 g.) was filtered off. Crystallisation from butan-1-ol gave *1 : 3 : 5-trimethoxy-2-xanthhydrylbenzene* (4·8 g., 68%), m. p. 159—161°. The m. p. was raised to 163—164° by further crystallisation from butan-1-ol (7 parts) (Found: C, 76·1; H, 6·1. $C_{32}H_{30}O_4$ requires C, 75·8; H, 5·8%).

Reaction of xanthhydryl chloride with phenylmagnesium bromide. A solution of xanthhydryl chloride (from xanthhydrol, 5·0 g.) in ether (30 ml.) was added dropwise to one of phenylmagnesium bromide (prepared from magnesium, 1·25 g.) in ether (50 ml.). The mixture was heated under reflux for 3 hr., then cooled and decomposed with 2N-sulphuric acid. The ethereal layer was separated, washed free from acid, dried, and evaporated. Benzene (5 ml.) was added to the residue and the crystalline product (2·8 g., 43%), m. p. 140—144°, filtered off in two crops. Crystallisation from ethanol (25 parts) gave 9-phenylxanthen, m. p. 146—147° (Found: C, 88·2; H, 5·6. Calc. for $C_{19}H_{14}O$: C, 88·35; H, 5·5%). Ullmann and Engi [5] give m. p. 145°.

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[*Received, August 25th*, 1958.]

[4] Sawicki and Oliverio, *J. Org. Chem.*, 1956, **21**, 183.
[5] Ullmann and Engi, *Ber.*, 1904, **37**, 2371.

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85. *Structure of Fulminate Ion.*

By KARTAR SINGH.

NEF [1] assigned a structure $\bar{O}$–N=C to fulminate ion. Pauling and Hendricks [2] suggested an alternative formula $\bar{C}$=N=O based on calculations of potential energy of three nuclei which suggested that $^-$CNO is the most stable configuration. Our infrared results for various fulminates rule out Nef's structure, and studies of ultraviolet absorption spectra

[1] Nef, *Annalen*, 1894, **280**, 263, 305; Wohler, *Ber.*, 1906, **39**, 2522.
[2] Pauling and Hendricks, *J. Amer. Chem. Soc.*, 1926, **48**, 641.

XUM

of fulminates and quantum mechanical calculations suggest that the most probable one is –$\bar{O}$–N≡C.

On thermal decomposition mercury fulminate gives an insensitive and insoluble product, pyrofulmin. Langhans,[3] on the basis of colour reactions, suggested that pyrofulmin is probably a mixture of mercury oxycyanide with mercuric oxide. Its insolubility makes it difficult to apply usual chemical methods to elucidate its structure, but its infrared and ultraviolet spectra in the solid phase establish the presence of –N=C=N– and –C≡N groups.

Mercury fulminate was purified by dissolving a fresh sample in aqueous ammonia followed by precipitation with 20% acetic acid and washing with water. Silver and lead fulminates were prepared as described in the literature.[4] Pyrofulmin was obtained by heating mercury fulminate at 88° ± 0·5° *in vacuo*. Samples decomposed to different extents were also examined.

FIG. 1.

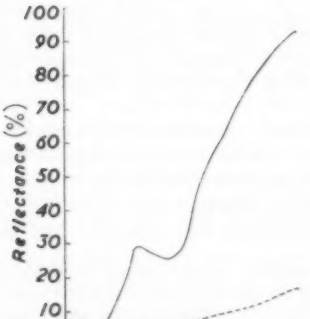
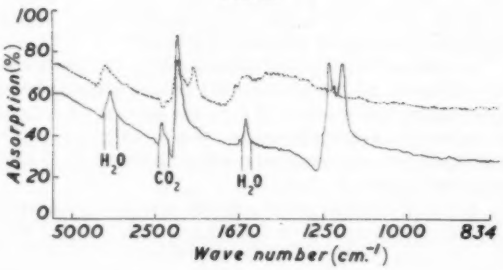


FIG. 2.



Infrared spectra (2—15 μ) were examined in potassium bromide discs [5] containing 0·7% of the sample (w/w) with a Hilger H 800 double-beam spectrograph. Ultraviolet absorption spectra were determined by reflections from pellets with a Hilger Uvispek Spectrophotometer No. H.700/304 (Fig. 1). Mercury fulminate (full line) shows two broad and intense absorption bands centred at 3310 Å and 2400 Å, and pyrofulmin (broken line) absorbs at the same positions but the bands are indistinct.

The positions of peaks in the infrared spectra of fulminates are given in Table 1. Peaks arising from adsorbed water [6] (near 3450 cm.$^{-1}$ and 1640 cm.$^{-1}$) and adsorbed carbon dioxide (near 2350 cm.$^{-1}$) were neglected.

TABLE 1. *Positions (cm.$^{-1}$) of infrared absorption peaks of fulminates.*

Fulminate	$2\nu_1$	ν_3	ν_1	$2\nu_2$
Mercury	—	2147vs	1225vs	1181s
Silver	2215s	2132vs	1123vs	1111s
Lead	—	2172vs	1188vs	—

The peaks at 1225 and 2147 cm.$^{-1}$ for mercury fulminate may respectively be the fundamental frequencies representing symmetric (ν_1) and antisymmetric (ν_3) vibrations of –ONC group, and

[3] Langhans, *Z. ges. Schiess- and Sprengstoffw.*, 1922, **17**, 122.
[4] Taylor and Rinkenbeck, *Army Ordnance*, 1926, **6**, 448; Wohler and Martin, *Ber.*, 1917, **50**, 586.
[5] Stimson and O'Donnel, *J. Amer. Chem. Soc.*, 1952, **74**, 1805.
[6] Brame, Margrave, and Meloche, *J. Inorg. Nuclear. Chem.*, 1957, **5**, 49.

that at 1181 cm.$^{-1}$ the bending frequency $2\nu_2$. The high intensity of this peak is obviously due to Fermi resonance. The position of peaks in the infrared spectra of products formed on heating mercury fulminate to various losses are in Table 2. The infrared spectra of products formed at losses of 0·1 (full line) and 10·2% (broken line) are given in Fig. 2. When mercury fulminate has lost 1·2% in weight a new peak appears at 1988 cm.$^{-1}$, whose intensity increases

TABLE 2. *Positions (cm.$^{-1}$) of infrared peaks of decomposition products of mercury fulminate.*

Loss in wt. (%)	ν_3	$'\nu_3$	ν_1	$2\nu_2$	Loss in wt. (%)	ν_3	$'\nu_3$
0·1	2187vs	—	1218vs	1152s	7·8	2135s	1987s
0·3	2202vs	—	1221vs	1178s	10·2	2155s	1987s
1·8	2199vs	1988vw	1221vs	1181s			

on continued heating up to a loss of 10·2%. The peaks at 1225 and 1181 cm.$^{-1}$ fade out completely at a loss of 10·2%. The peak at 2147 cm.$^{-1}$ remains practically unaltered in position.

The three possible canonical structures for the fulminate ion are (I), (II), and (III). Preponderance of structure (I) implies an infrared absorption at about 1670 cm.$^{-1}$. Absence of infrared absorption signifies that structure (I) does not make a large contribution.

Nef Pauling and Hendricks

(I) (II) (III) (IV)

The observed values of symmetrical and antisymmetrical vibrations are comparable with those of carbon dioxide O=C=O [7] or to those of 2 : 4 : 6-trimethylbenzonitrile oxide which has been assigned [8] the structure (IV; R = 2 : 4 : 6-$Me_3C_6H_2$). The infrared spectra alone, therefore, do not provide definite evidence whether structure (II) or (III) or a resonance hybrid makes a major contribution. The presence of a strong, broad band centred at 3310 Å, probably arising from $\eta \longrightarrow \pi^*$ transitions,[9,10] indicates that structure (III) may predominate. A firm decision requires well-resolved ultraviolet band spectra and their quantitative interpretation.

The presence of peaks at 1987 cm.$^{-1}$ and 2155 cm.$^{-1}$ in the spectrum of pyrofulmin indicates that $-N=C=N-$ and $-C\equiv N$ groups may be present.

I thank Professors D. S. Kothari and C. H. Smith for encouragement.

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[7] Mulligan, *J. Chem. Phys.*, 1951, **19**, 347.
[8] Califano, Moccia, Scarpate, and Speroni, *ibid.*, 1957, **26**, 1727.
[9] Trawick and Eberhardt, *ibid.*, 1954, **22**, 1162.
[10] Ito, Shimada, Kuraishi, and Mizushima, *ibid.*, 1957, **26**, 1508.

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86. *The Rearrangement of Nitrones.*

By A. H. WRAGG and T. S. STEVENS.

MARTYNOFF [1] observed the formation of *O*-(*o*-methoxydiphenylmethyl)benzaldoxime, MeO·C_6H_4·CHPh·O·N:CHPh, as a by-product in the acid hydrolysis of the *N*-isomer, MeO·C_6H_4·CHPh·$\overset{+}{N}(\bar{O})$:CHPh, and concluded that it arose by direct radical migration from nitrogen to oxygen. We had begun a general study of nitrones in order to define the

[1] Martynoff, *Ann. Chim.*, 1937, **7**, 424.

XUM

incidence of this analogue of the Meisenheimer rearrangement of amine oxides, when Cope and Haven [2] brought about the thermal rearrangement of *N*-diphenylmethylbenzophenone oxime, $Ph_2CH{\cdot}\overset{+}{N}(\bar{O}){:}CPh_2$, but not that of *N*-benzylbenzophenone oxime. Our preliminary observations are now reported.

Rearrangement was not observed in the thermal treatment, under a variety of conditions, of *N*-phenyl-, *N*-benzyl-, *N*-diphenylmethyl-, or *N*-cinnamyl-benzaldoxime. The two first gave, respectively, some benzanilide and some *N*-benzylbenzamide, which could be products of a Beckmann change. *N*-9-Fluorenylhydroxylamine was prepared, but in insufficient quantity for the preparation and study of 9-fluorenylnitrones.

Grammaticakis,[3] Martynoff, and Cope and Haven all regarded the production of hydroxylamine in the acid hydrolysis of the *N*-derivative of an oxime as good evidence of rearrangement to the *O*-derivative, followed by hydrolysis:

$$R{\cdot}\overset{+}{N}(\bar{O}){:}CR_2' \longrightarrow R{\cdot}O{\cdot}N{:}CR_2' \longrightarrow R{\cdot}O{\cdot}NH_2 + COR_2'$$
$$\downarrow$$
$$HO{\cdot}NH_2$$

This conclusion is not always valid, for *N*-diphenylmethylhydroxylamine is hydrolysed under relatively mild conditions to hydroxylamine and bisdiphenylmethyl ether.

Experimental.—N-*Phenylbenzaldoxime.*[4] This nitrone (0·762 g.) was heated at 200° for 1 hr. Steam distillation then gave benzaldehyde which yielded the 2 : 4-dinitrophenylhydrazone (1·007 g.), m. p. and mixed m. p. 235°; the residue afforded benzanilide (mixed m. p.) (46 mg.).

N-*Benzylbenzaldoxime.*[5] This was prepared by oxidising *NN*-dibenzylhydroxylamine (50 g.) in chloroform (450 ml.) with yellow mercuric oxide (60 g.) with shaking and cooling. The product (46·5 g.) was crystallised from ethanol–ligroin (b. p. 60—80°). *NN*-Dibenzylhydroxylamine [6] was obtained from hydroxylamine hydrochloride (42 g.), benzyl chloride (144 g.), and sodium carbonate (110 g.), in refluxing water (200 ml.)–ethanol (1000 ml.) for 6 hr. Ethanol was distilled off, water added, and the precipitate crystallised twice from ethanol to give large crystals. The small crystals of tribenzylamine (mixed m. p.) were washed out with ether and the product was again crystallised from ethanol; it had m. p. 123°.

In three experiments, *N*-benzylbenzaldoxime was heated at 150° for 8 hr., at 190° for 3 hr., and distilled under 15 mm. pressure. In each case the product was heated with phenylhydrazine at 107—110° for 8 hr. to liberate *N*- and possibly *O*-benzylhydroxylamine; after *N*-benzylhydroxylamine and unchanged phenylhydrazine had been destroyed by Fehling's solution, no *O*-benzylhydroxylamine could be recognised. When 10% of *O*-benzylbenzaldoxime [7] was added to this initial material in parallel experiments *O*-benzylhydroxylamine was easily recognised and characterised as *O*-benzyl-*p*-nitrobenzaldoxime [8] (mixed m. p.) (Found: N, 11·0. Calc. for $C_{14}H_{12}O_3N_2$: N, 10·9%).

N-*Diphenylmethylbenzaldoxime.* *N*-Diphenylmethylhydroxylamine oxalate [9] (6·1 g.), m. p. 185° (decomp.), benzaldehyde (2·65 g.), and hydrated sodium acetate (3·4 g.) in ethanol (100 ml.) were refluxed for 2 hr., affording *N*-diphenylmethylbenzaldoxime (6·3 g.), as needles, m. p. 159—160°,[5] from ethanol. The nitrone (6 g.) was heated at 170° for 3 hr. From the melt, acid extracted diphenylmethylamine (1·22 g.), identified as hydrochloride and as *p*-nitrobenzylidene derivative (mixed m. p.s); no *O*-diphenylmethylhydroxylamine could be recognised by the procedure reported above. Distillation of *N*-diphenylmethylbenzaldoxime (6 g.) at 17 mm.

[2] Cope and Haven, *J. Amer. Chem. Soc.*, 1950, **72**, 4896.
[3] Grammaticakis, *Compt. rend.*, 1937, **205**, 60.
[4] Bamberger, *Ber.*, 1894, **27**, 1556.
[5] Angeli, Alessandri, and Aiazzi-Mancini, *Atti reale Accad. Lincei*, 1911, **20**, I, 546.
[6] Behrend and Leuchs, *Annalen*, 1890, **257**, 216.
[7] Beckmann, *Ber.*, 1889, **22**, 514.
[8] Behrend and König, *Annalen*, 1891, **263**, 353.
[9] Platner, *ibid.*, 1894, **278**, 364.

pressure gave *sym.*-tetraphenylethane (mixed m. p.; 1·3 g.) and diphenylmethylamine (0·6 g.); this was identified as before. N-*Diphenylmethyl*-p-*nitrobenzylideneamine*, needles (m. p. 135°) from ethanol, was also prepared from diphenylmethylamine hydrochloride and *p*-nitrobenzaldehyde with sodium acetate in boiling alcohol (3 hr.) (Found: C, 76·0; H, 5·2; N, 8·7. $C_{20}H_{16}O_2N_2$ requires C, 76·0; H, 5·1; N, 8·7%).

N-*Cinnamylbenzaldoxime*. Cinnamyl bromide (22·5 g.), acetoxime (12·5 g.), acetic acid (25 ml.), and water (8 ml.) were boiled for 30 min. and then evaporated quickly to half the bulk (cf. ref. 9). After addition of water, the mixture was extracted thoroughly with ether and the aqueous layer treated with ammonium oxalate. The precipitated N-*cinnamylhydroxylamine oxalate* (8 g.) crystallised from 90% ethanol in plates, m. p. 177—178° (decomp.) (Found: C, 61·75; H, 5·9; N, 7·4. $C_{20}H_{24}O_6N_2$ requires C, 61·9; H, 6·2; N, 7·2%). The oxalate (6 g.), benzaldehyde (3·4 g.), and hydrated sodium acetate (4·25 g.) in ethanol (100 ml.) were refluxed for 3 hr., affording N-*cinnamylbenzaldoxime* as needles, m. p. 73°, from ether–ligroin (b. p. 40—60°) (Found: C, 80·8; H, 6·4; N, 5·4. $C_{16}H_{15}ON$ requires C, 81·1; H, 6·3; N, 5·9%). When the nitrone was heated at 138° for 2 hr., or distilled at 19—20 mm. pressure, it decomposed extensively, the only definable product being benzaldehyde.

9-Bromofluorene (5 g.), treated with acetoxime (1·49 g.) in acetic acid (75%; 20 ml.) as in the previous instance, gave variable yields (*ca.* 20%) of N-9-*fluorenylhydroxylamine oxalate*, as plates, m. p. 205° (decomp.), from ethanol (Found: C, 70·0; H, 5·0; N, 5·6. $C_{28}H_{24}O_6N_2$ requires C, 69·5; H, 5·0; N, 5·8%).

Hydrolysis of N-*diphenylmethylhydroxylamine*. The base (2·4 g.) in 12% hydrochloric acid (50 ml.) was heated on a boiling-water bath for 4 hr. Ether then extracted bis(diphenylmethyl) ether (mixed m. p.). Evaporation of the acid solution gave a solid, part of which dissolved in chloroform and was the hydrochloride of the unchanged base. The insoluble portion (0·48 g.) was recognised as hydroxylamine hydrochloride (Found: Cl, 50·6. Calc. for NH_4OCl: Cl, 51·0%) by the spot test with salicylaldehyde and copper acetate [10] and by conversion into benzophenoneoxime (mixed m. p.).

The authors thank the Sheffield Town Trustees for a Scholarship (to A. H. W.).

THE UNIVERSITY, SHEFFIELD, 10. [*Received, June 10th*, 1958.]

[10] Feigl, *Rec. Trav. chim.*, 1939, **58**, 475.

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87. *Steric Effects and Hydrogen Isotope Exchange in* 1 : 2 : 3-*Trimethoxybenzene.*

By D. P. N. SATCHELL.

WHILE investigating [1] the rate of aromatic hydrogen isotope exchange between [4 : 6-^{3}H]1 : 2 : 3-trimethoxybenzene and aqueous solutions of weak acids, we wished to show that the exchange rate for this compound in aqueous solutions of strong mineral acids was determined by Hammett's acidity function, as it is for all neutral aromatic compounds so far studied.[2] The rate of exchange was examined at three acidities in aqueous sulphuric acid. This strong acid was chosen because the behaviour of anisole has been studied quantitatively in it; [2] this study, coupled with that of Melander and Olsson [3] on the isotope effect in aromatic hydrogen exchange, makes possible a moderately quantitative prediction of the exchange rate of 1 : 2 : 3-trimethoxybenzene, it being assumed that the activating effects of substituents in the ring are independent and additive.[4]

The measured exchange-rate constants, λ, and the H_0 data are in the Table. log λ

[1] Satchell, *J.*, 1958, 3904.
[2] Satchell, *J.*, 1956, 3911 and references therein.
[3] Melander and Olsson, *Acta. Chem. Scand.*, 1956, **10**, 879.
[4] (*a*) Bradfield, *Trans. Faraday Soc.*, 1941, **37**, 726; (*b*) Jones, *J.*, 1942, 418, 1676; (*c*) Condon, *J. Amer. Chem. Soc.*, 1948, **70**, 1963; (*d*) de la Mare and Vernon, *J.*, 1951, 1764; (*e*) de la Mare and Hassan, *J.*, 1958, 1519.

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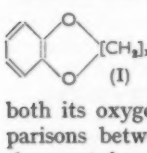
is linearly related to H_0, with a slope close to unity, as expected. However, the observed exchange rate at, say, 4·7M, is about sixty-fold slower than that predicted. The prediction admittedly involves some assumptions apart from that of the methoxyl substituents' contributing independently and additively to the activation energy.

First-order exchange rate in aqueous sulphuric acid at 25°.

	(*a*) [4 : 6-^{3}H]1 : 2 : 3-Trimethoxybenzene			(*b*) [4 : 6-^{3}H]2-Hydroxy-1 : 3-dimethoxybenzene	
H_2SO_4 (M)	3·51	4·70	5·22	4·70	5·22
$-H_0$	1·62	2·15	2·37	2·15	2·37
$10^4\lambda$ (sec.$^{-1}$)	0·52	1·75	2·91	3·00	5·06

It is first assumed that the exchange data for benzene in aqueous sulphuric acid [2] may be extrapolated to 4·7M (*ca.* 3 H_0 units), so that the appropriate *ortho*- and *para*-partial rate factors for anisole can be calculated. This extrapolation seems unlikely to lead to great error.[2] Secondly, the previous data apply to deuterium exchange whereas the present rates concern tritium. An isotope rate ratio has, therefore, to be assumed. Melander and Olsson found this ratio, λ_T/λ_D, for exchange in toluene to be *ca.* 0·5. No great error is likely to be introduced by assuming the value for 1 : 2 : 3-trimethoxybenzene to be about the same. Thirdly, a value for the *meta*-partial rate factor of anisole has to be assumed. It is *ca.* 0·25 in strong perchloric acid, and probably much the same in strong sulphuric acid.[2] However, the trends of the graphs in ref. 2 imply that, if anything, the deactivation will decrease as the acidity decreases. (Results for other types of reaction with dimethoxybenzenes indicate *activation* of the *meta*-position.[2]) Hence the assumption of a value of 0·2 seems well on the safe side. It is considered that the above assumptions, which lead to an expected rate of *ca.* $1{\cdot}0 \times 10^{-2}$ sec.$^{-1}$ for the 4- and the 6-position of [4 : 6-^{3}H]1 : 2 : 3-trimethoxybenzene, are not likely to involve a greater total error than a factor of 3 or 4. The observed exchange rate is, in fact, 57-fold slower than predicted. It seems clear that the three methoxyl groups are *not* activating the ring independently and additively, and some form of steric interaction seems probable.[4e]



(I)

Neighbouring methoxyl groups, and methoxyl groups flanked by other substituents, have been studied before from the steric viewpoint.[5] The general conclusions are as follows. First, for the methoxyl group to exert its maximum accelerative effect on electrophilic aromatic substitution, both its oxygen and carbon atoms should lie in the plane of the ring. Secondly, comparisons between the reactivity of veratrole and compounds of type (I) indicate that the most favoured disposition of the oxygen–carbon bonds is *trans–trans*. It has been suggested [5b] that in this position the lone pair of electrons on one oxygen atom can interact electrostatically with the positive charge developed on the other on assuming its quinonoid form. It is possible that this extra stabilisation, available in veratrole but not in anisole, explains the seeming discrepancy between partial rate factors deduced for the latter from experiments with the former, and the directly determined partial rate factors.[2] Thirdly, there is evidence that when both positions *ortho* to a methoxyl group are occupied, the group has difficulty in assuming the most favourable, planar configuration.

The above considerations apply to the influence of steric requirements on the methoxyl group's mesomeric activation of the ring. The plane of the carbon–oxygen–carbon bond is probably less important in determining the (deactivating) inductive effect of the group.

The 4- and the 6-position are the reactive sites in 1 : 2 : 3-trimethoxybenzene. Their powerful activation is provided by the 1- and the 3-methoxyl group and is (perhaps) moderated by the 2-substituent. Steric considerations lead to the conclusion that, for three adjacent methoxyl groups, only the 1- and the 3-substituent can lie easily and

[5] (*a*) Brown, Wilzbach, and Urry, *Canad. J. Res.*, 1949, **27**, *B*, 398; (*b*) Baddeley, Holt, Smith, and Whittaker, *Nature*, 1951, **168**, 386; (*c*) Baddeley and Smith, *ibid.*, 1949, **164**, 1014; (*d*) Baddeley, Smith, and Vickars, *J.*, 1956, 2455; (*e*) Horton and Rossiter, *J. Org. Chem.*, 1958, **23**, 488.

simultaneously in the plane of the ring, *i.e.*, in their positions most favourable mesomerically for reactivity. To do so they must take up the *trans–trans* position, interaction with the neighbouring oxygen atom discouraging the *cis–trans* or *cis–cis* configuration. The 2-substituent cannot easily lie in the plane of the ring.

These points being borne in mind, there seem two possible reasons for the unexpectedly low reactivity of the 4- and the 6-position. (1) The net effect of the 2-substituent on the reaction centres *meta* to it is doubtless due to a balance between its $-I$ effect and any second-order relay of its $+T$ effect.[6] The loss of conjugation by this group must reduce the latter, and thus deactivate the 4- and the 6-position if the inductive effect is unaffected, as it may be. This influence is, however, even by description, a second-order effect, and likely to be small. This is supported by experiments with 2-hydroxy-1 : 3-dimethoxybenzene described below. (2) The presumed *trans–trans* orientation of the 1- and the 3-substituent, at least at the moment of reaction, will shield the 4- and the 6-position, and to some extent hinder the approach of the reagent. Possibly this effect is appreciable, and it is considered that it probably accounts for most of the loss of reactivity. Thus, for 1 : 2 : 3-trimethoxybenzene, it is concluded that direct steric shielding of the reaction centres is more important than any sterically induced loss of mesomerism.

The rate of tritium exchange at the 4- and the 6-position of 2-hydroxy-1 : 3-dimethoxybenzene was also measured in aqueous sulphuric acid, and is included in the Table. The rate is faster than for trimethoxybenzene by a factor of *ca.* 1·7. For the 2-hydroxy-compound steric considerations indicate that all the substituents can lie in the plane of the ring, though the factor which chiefly influences the orientation of the 4- and the 6-substituent, namely the adjacent oxygen atom, remains unchanged, so that little change in steric hindrance due to these groups is to be expected—and if anything a reduction.

The hydroxyl group possesses inductive and mesomeric effects similar in magnitude to those of a methoxyl group.[7] The $+T$ effect seems a little more,[2] and the $-I$ effect a little less,[8] powerful than for the latter group. The absence of any steric inhibition of mesomerism for the hydroxyl group will therefore produce a second-order relay, at the 4- and the 6-position, comparable to that which the 2-methoxyl group of 1 : 2 : 3-trimethoxybenzene would produce if it could assume coplanarity. The inductive deactivation will be comparable, if a little less. Hence an increase in reactivity for the 2-hydroxy-compound is to be expected from three sources, all of which are likely to be small. The fact that they *are* small is proved by the rate factor of only 1·7. It seems clear (as was assumed above) that the steric reduction of second-order relay can play only a minor part in determining the reactivity of the 4- and the 6-position in trimethoxybenzene.

Experimental.—Tritiated compounds. The preparation of the [4 : 6-^{3}H]1 : 2 : 3-trimethoxybenzene has been described.[1] The labelled 2-hydroxy-1 : 3-dimethoxybenzene was prepared by solution of the light compound in 24·4 moles % ethanol–THO, containing hydrogen chloride, and of known [9] H_0. After a period based on the expected exchange rate for the 4- and the 6-position (the 5-position must be *ca.* 10^4 times less active) at 25°, the solution was partly neutralised with sodium hydroxide, diluted with water, and extracted with ether. Evaporation of the ether, followed by recrystallisation, gave a product of m. p. 36°. The hydroxyl group of the main product was not rigorously freed from significant tritium, since in the kinetic experiments the large excess of solvent automatically accomplished this. A small portion was so freed for use as the sample representing zero exchange time. Its activity showed that exchange equilibrium had not been reached for the 4- and the 6-position, and therefore the 5-position was doubtless free from tritium.

Exchange experiments. These were conducted under homogeneous conditions at 25°. Samples (~0·08 g.) were dissolved in 100 ml. samples of acid mixture in flasks fitted with ground

[6] Baker, Barrett, and Tweed, *J.*, 1952, 2833.
[7] Rosenwald, *J. Amer. Chem. Soc.*, 1952, **74**, 4602.
[8] Badger, "Structures and Reactions of the Aromatic Compounds," Cambridge Univ. Press, 1954, p. 190.
[9] Satchell, *J.*, 1957, 3524.

XUM

glass stoppers, and immersed in a thermostat bath. Flasks were removed after known intervals, and their contents diluted with water and extracted with ether. Evaporation of the ether left crystalline material of good m. p., the activity of which was determined as previously described.[1]

The methoxyl groups of both the 1 : 2 : 3-trimethoxy- and the 1 : 2-dimethoxy-compounds should be stable in the acid mixtures used.[10]

H_0 data are taken from Paul and Long.[11] Those in ref. 2 were not.

This work was performed under the auspices of the U.S. Atomic Energy Commission.

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[*Present Address.*—KING'S COLLEGE, LONDON, W.C.2.] [*Received, June 16th,* 1958.]

[10] Burwell, *Chem. Rev.*, 1954, **54**, 615.
[11] Paul and Long, *Chem. Rev.*, 1957, **57**, 1.

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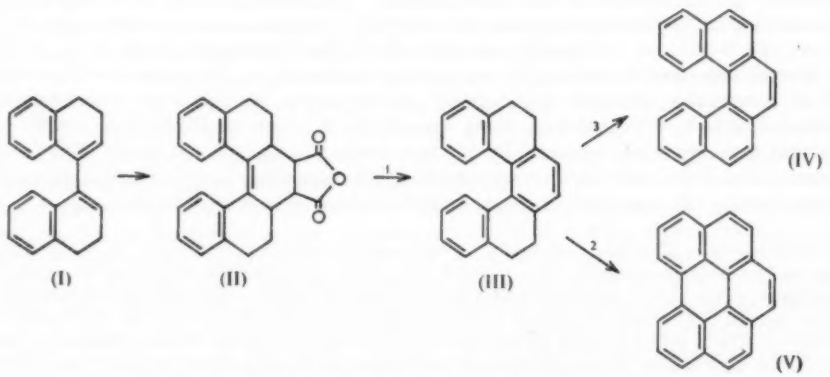
88. *Alicyclic Studies. Part XIV.*[1] *An Improved Synthesis of 3 : 4-5 : 6-Dibenzophenanthrene and 1 : 12-Benzoperylene.*

By YANINA ALTMAN and DAVID GINSBURG.

IT appeared from our work on symmetrical alicyclic dienes [1] that the existing syntheses of 3 : 4-5 : 6-dibenzophenanthrene [2-4] could be improved. This compound has been synthesised in 23% overall yield based on α-tetralone as starting material, the lead dioxide oxidative–decarboxylation procedure [5,6] being employed on the intermediate (II). Bromination-dehydrobromination of the product (III) afforded the required hydrocarbon (IV).



Reagents: 1, PbO_2. 2, Pd–C. 3, *N*-Bromosuccinimide, then NaOAc.

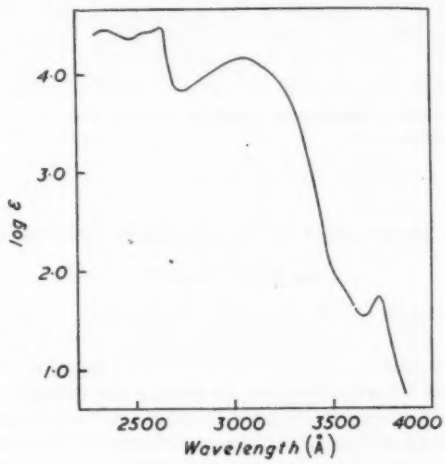
Alternatively, dehydrogenation of compound (III) with palladised carbon afforded 1 : 12-benzoperylene (V) in 95% yield, an improvement over previous syntheses of this hydrocarbon.[7,8]

[1] Part XIII, Greidinger and Ginsburg, *J. Org. Chem.*, 1957, **22**, 1406.
[2] Weidlich, *Ber.*, 1938, **71**, 1203.
[3] Cook, *J.*, 1933, 1592.
[4] E. D. Bergmann and Szmuszkovicz, *J. Amer. Chem. Soc.*, 1951, **73**, 5153.
[5] Doering and Farber, *ibid.*, 1952, **74**, 4370.
[6] Doering and Finkelstein, *J. Org. Chem.*, 1958, **23**, 141.
[7] Clar, *Ber.*, 1932, **65**, 846.
[8] Hewett, *J.*, 1938, 1286.

The ultraviolet absorption spectrum of compound (III) is reproduced in the Figure. The spectra of compounds (IV) and (V) were superimposable, respectively, upon those already published.[4, 7]

Experimental.—3 : 4 : 3′ : 4′-*Tetrahydro*-1 : 1′-*dinaphthyl* (I). A mixture of freshly scraped aluminium foil (6 g.; 0·005 in. thickness, 1 sq. cm. squares), α-tetralone (21 g.), dry ethanol (150 ml.), dry benzene (100 ml.), and mercuric chloride (0·5 g.) was heated on the steam-bath for 14 hr. After cooling, the excess of aluminium was dissolved in cold 10% hydrochloric acid. The aqueous phase was extracted with benzene–ether (1 : 1), and the combined organic phases were washed once with dilute hydrochloric acid. The solvents were removed and a mixture of acetic acid (45 ml.) and acetic anhydride (45 ml.) was added to the residue and dehydration of the pinacol was completed by boiling for 2 hr. Concentration of the solution to a small volume afforded the diene (15 g., 81%), m. p. 138—140°, which was sufficiently pure for the next step. It had m. p. 141° (from ethanol) (lit.,[2, 9] m. p. 141°).

Spectrum of 1 : 2 : 7 : 8-*tetrahydro*-3 : 4-5 : 6-*dibenzophenanthrene in* cyclo*hexane.*



1 : 2 : 7 : 8 : 8a : 9 : 10 : 10a-*Octahydro*-3 : 4-5 : 6-*dibenzophenanthrene*-9 : 10-*dicarboxylic anhydride* (II). On the steam-bath maleic anhydride (24 g.) and the above diene (6 g.) gave a melt which began depositing crystals after 30 min. After 4 hours' heating, the solid formed was dissolved in hot acetic acid. Concentration and cooling gave the *anhydride* (6·2 g., 75%), m. p. 252—254°. Recrystallisation from toluene raised the m. p. to 256° (lit.,[2, 9] m. p. 254°, 256°). A 95% yield of crude adduct has been reported.[9]

1 : 2 : 7 : 8-*Tetrahydro*-3 : 4-5 : 6-*dibenzophenanthrene* (III). A finely powdered mixture of the anhydride (500 mg.) and lead dioxide (1·34 g.; Fisher, technical grade) and freshly distilled decalin (4 ml.) were placed in a 25 ml. flask equipped with gas-inlet tube leading to the surface of the reaction mixture and an outlet tube leading into a solution of barium hydroxide. The temperature was gradually raised to 190—200° and the mixture was kept in an inert atmosphere. Carbon dioxide was evolved during *ca.* 3 hr. The mixture was cooled to 100°, 2 : 2 : 4-trimethylpentane was added, and reflux was maintained for 10 min. The liquid was decanted and this procedure was repeated twice. Finally the solid was removed and washed with ether. All of the extracts were united and the solvents were removed in a vacuum. The residual oil was triturated with pentane, giving brown prisms (165 mg., 41%). Sublimation at 140—150°/0·05 mm. gave the colourless hydrocarbon (160 mg.), m. p. 144—146°. Recrystallisation from ethanol gave prismatic rosettes, m. p. 148—149° (lit.,[2] 142°). 43% of the theoretical quantity of carbon dioxide was isolated as barium carbonate.

[9] F. Bergmann, Eschinazi, and Neeman, *J. Org. Chem.*, 1943, **8**, 179.

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With specially prepared lead dioxide [6] the yield fell to 15%. When powdered Pyrex glass was used instead of decalin, together with double the quantity of lead dioxide,[6] the yield was 30—32%.

3 : 4-5 : 6-*Dibenzophenanthrene* (IV). A mixture of the above hydrocarbon (227 mg.), *N*-bromosuccinimide (284 mg.), dibenzoyl peroxide (14 mg.), and dry carbon tetrachloride (10 ml.) was refluxed for 30 min. Much hydrogen bromide was evolved. Acetic acid (4 ml.) and sodium acetate (0·82 g.) were added and heating was continued for 1 hr. After cooling, water was added and the organic layer was separated and washed with water, sodium hydrogen carbonate solution, and again water. After drying (Na_2SO_4) and removal of the solvent, the yellow residue was dissolved in benzene (2 ml.)–hexane (1 ml.), and the solution was filtered through a column of basic alumina (15 g.) and eluted with benzene–hexane (2 : 1). Removal of solvents from the eluate afforded the light yellow aromatic hydrocarbon (220 mg.), m. p. 176°. Crystallisation from ethanol (charcoal) gave colourless material, m. p. 178° (204 mg., 92%). Crystallisation from ethanol with rapid cooling gave glistening platelets. Slow crystallisation from hexane gave yellowish prisms whilst slow crystallisation from ethanol gave both needles and rosette-shaped feathers (lit.,[3-4] m. p. 177°, 177—178°).

1 : 12-*Benzoperylene* (V). A mixture of the hydrocarbon (III) (60 mg.), 30% palladised carbon (40 mg.), and *p*-cymene (5 ml.) was heated under reflux for 5 hr. in an inert atmosphere. Cooling and removal of the catalyst and the solvent afforded a yellow residue of 1 : 12-benzoperylene (57 mg.), m. p. 273° (from propan-1-ol) (lit.,[7, 8] m. p. 273°, 269—270°).

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89. *The Extractives of* Dysoxylum spectabile, *Hook.*

By R. C. CAMBIE.

Dysoxylum spectabile Hook. (New Zealand "Kohekohe"; family, Meliaceae) is the only species of the genus found in New Zealand and is endemic, the tree being restricted to the coastal and semi-coastal forests of North Island and the northern part of South Island. The aim of the investigation was to isolate the (possibly crystalline) pigments which were responsible for the strong reddish colour of the heartwood. Extraction of the heartwood and the bark with light petroleum, followed by chromatography on alumina, gave β-sitosterol as the principal sterol present, in 0·014% and 0·017% yield respectively. As mixed-melting-point determinations are unreliable for sitosterols,[1] characterisation was by means of the acetate. Other sterols probably present in the heartwood extract, as indicated by positive Liebermann–Burchard and Nath [2] tests, were not present in sufficient quantity for purification.

Extraction of the bark with ether gave a non-phenolic oil, chromatography of which on alumina gave no useful results. Saponification, followed by chromatography of the unsaponifiable fraction, however, gave an impure but crystalline ketone in a yield (0·002%) that was insufficient to permit further examination. Preliminary examination showed that ether gave a negligible extract from the heartwood.

Alcoholic extracts of both the heartwood and the bark were deep red but were mainly composed of condensed tannins, as indicated by a variety of reagents.[3] The tannin fractions which were responsible for the colour did not melt and had zero R_F in all chromatographic systems tried. They were not readily purified and were not investigated further. Paper chromatography of the heartwood extract showed the presence of a single further phenolic compound which was isolated by chromatography of an ethyl acetate extract on a

[1] Fieser and Fieser, "Natural Products Related to Phenanthrene," Reinhold Publ. Corpn., New York, 1949, p. 286.
[2] Nath, *Ann. Biochem. Exp. Med.*, 1942, **2**, 83; *Chem. Abs.*, 1943, **37**, 3701.
[3] Russell, *Chem. Rev.*, 1935, **17**, 165; Michaluk, *Acta Polon. Pharm.*, 1954, II, 362; *Chem. Abs.*, 1955, **49**, 9948.

cellulose column. It was identified as (+)-catechin by comparison with an authentic sample. It was not detected in the bark by paper chromatography. Tests indicated absence of flavonoids,[4] anthocyanins,[4] *leuco*anthocyanins,[5] and alkaloids from extracts of both the bark and the heartwood.

Experimental.—Microanalyses were by Dr. A. D. Campbell, University of Otago, N.Z. Infrared spectra were measured on potassium bromide discs and ultraviolet spectra were measured for ethanolic solutions.

(a) *The heartwood; β-sitosterol.* Finely milled heartwood (720 g.) was extracted (Soxhlet) with light petroleum (b. p. 56—62°) for 90 hr. Chromatography of the waxy concentrate (170 mg.) in benzene on neutralised alumina and recrystallisation of the major product as plates from aqueous methanol gave β-sitosterol, m. p. and mixed m. p. 134—135° [Found: for sample dried at room temperature: C, 80·3, 80·4; H, 12·7, 12·3%; *M* (Rast), 436. Calc. for $C_{29}H_{50}O,H_2O$: C, 80·5; H, 12·1%; *M*, 433. Found, for sample dried at 100°: C, 84·1; H, 12·6. Calc. for $C_{29}H_{50}O$: C, 84·0; H, 12·2%], $\lambda_{max.}$ 207 mμ (log ε 3·61) [Wheeler and Mateos [6] record 207 mμ (ε 4200)], $\nu_{max.}$ 3436 (bonded OH), 2950 (C–H), 2857 (C–H), 1684 (Δ^5-ethylenic bond) cm.$^{-1}$. The acetate, prepared by the use of pyridine and acetic anhydride (1 hr.; 90°), formed plates (from methanol), m. p. and mixed m. p. 127—128° (Found: C, 81·9; H, 11·6. Calc. for $C_{31}H_{52}O_2$: C, 81·5; H, 11·5%).

(+)-*Catechin.* The air-dried heartwood was further extracted with ethanol for 9 hr. and tannins (50 g.) were precipitated from the syrupy concentrate by the addition of ether. The filtrate was extracted with saturated sodium hydrogen carbonate, and the extract acidified. Chromatography of an ethyl acetate extract of the precipitate, on a cellulose column, gave a discoloured fraction (261 mg.), circular R_F 0·41 in phenol–water (9 : 1), 0·73 in 40% acetic acid. Repeated crystallisation from hot water (charcoal) gave colourless needles of (+)-catechin, m. p. and mixed m. p. 175—176° with sintering at 149—150° (Found, for sample dried at 100°: C, 61·7; H, 4·9. Calc. for $C_{15}H_{14}O_6$: C, 62·1; H, 4·9%), $[\alpha]_D^{25}$ +17° [*c* 0·8 in Me_2CO–H_2O (1 : 1)], $\lambda_{max.}$ 280 mμ (log ε 3·62), $\nu_{max.}$ 3401 (OH), 3322 (OH), 2985 (C–H), 1626 (H_2O), 1618 (aromatic) cm.$^{-1}$. The penta-acetate, prepared by the use of pyridine and acetic anhydride, formed elongated prismatic rods (from methanol), m. p. 131—132° (Found: C, 59·8; H, 4·8; Ac, 41·8. Calc. for $C_{25}H_{24}O_{11}$: C, 60·0; H, 4·8; 5Ac, 42·3%).

Chromatography of the ether solution remaining after extraction with sodium hydrogen carbonate, on alumina, gave further β-sitosterol (10 mg.).

(b) *The bark.* Finely milled bark (1·025 kg.) was extracted (Soxhlet) with light petroleum for 24 hr. and the waxy concentrate chromatographed in benzene or alumina (Brockmann II). Recrystallisation, from methanol, of the fractions eluted with benzene–ether gave needles of β-sitosterol, m. p. and mixed m. p. 137—138° (Found: C, 84·2; H, 11·8%) (identical infrared spectrum). The acetate had m. p. and mixed m. p. 127—128° (Found: C, 81·4; H, 11·4%).

The bark was re-extracted with ether for 24 hr. and the brown oily concentrate (9·8 g.) hydrolysed with 2N-ethanolic potassium hydroxide for 6 hr. The unsaponifiable fraction was chromatographed in benzene on alumina (Brockmann II). Elution with benzene, benzene–ether, and ether gave yellow oils. From the fractions eluted with ethyl acetate a colourless fraction was obtained which separated from ethyl acetate as granular crystals (25 mg.), m. p. 89—90° (Found: C, 74·2; H, 12·2%), $\lambda_{max.}$ 273 mμ, $\nu_{max.}$ 2959 (CH_3), 2899 (CH_2), 1712 (C:O) cm.$^{-1}$. The substance gave positive tests for the carbonyl group but a negative Fehling's test.

A methanol extract of the bark (24 hr.) gave condensed tannins (10 g.), insoluble in ethyl acetate or water.

The author thanks Professor L. H. Briggs for suggesting this investigation and for interest in the work.

Department of Chemistry,
University of Auckland, New Zealand. [*Received, July 14th*, 1958.]

[4] Geissman in "Modern Methods of Plant Analysis," Springer-Verlag, Berlin, 1955, Vol. III, pp. 450—498.
[5] Bate-Smith and Lerner, *Biochem. J.*, 1954, **58**, 126.
[6] Wheeler and Mateos, *J. Org. Chem.*, 1956, **29**, 1110.

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90. *Chemistry of the* Coprosma *Genus. Part XI.* The Colouring Matters from* Coprosma foetidissima.

By E. G. Brooker.

Coprosma foetidissima [1] is a widely occurring, small shrub or tree endemic to New Zealand. All portions of the plant give a strong fœtid odour when bruised and methanethiol has been identified in a steam-distillate of the leaves.[2] The inner aerial bark is bright yellow and contains asperuloside.[3] Examination of a light petroleum extract of the aerial bark indicated the presence of three anthraquinones in insufficient amounts for identification. Further extraction with benzene gave a brown gum containing traces of anthraquinones, and an ether-extract contained traces of anthraquinones, rutin, and quercetin. Extraction with methanol yielded a brown gum from which rutin was obtained in 9·6% yield. Hydrolysis of the rutin mother-liquors indicated the presence of asperuloside but attempted isolation of asperuloside from unhydrolysed mother-liquors by Trim and Hill's procedure [4] did not yield sufficient material for identification. Rutin has been isolated from the root-bark of *Coprosma rhamnoides*.[5]

Experimental.—The analysis was carried out by Dr. A. D. Campbell, University of Otago. Anthraquinones were chromatographed in acetone over magnesium oxide. Paper chromatography of rutin and quercetin was carried out on Whatman No. 1 discs with aqueous acetic acid (1 : 13 v/v and 1 : 4 v/v, respectively) as developing solvents and ammonia vapour to locate the spots.

Air-dried aerial bark of *Coprosma foetidissima*, collected at Tongariro National Park in January, was extracted (Soxhlet) successively with light petroleum (b. p. 50—65°), benzene, ether, and methanol. The bright orange gum extracted by light petroleum gave colour reactions with concentrated sulphuric acid and aqueous alkali indicating the presence of anthraquinones. Chromatography over magnesium oxide gave three bands (upper band blue, middle band pink, and lower band yellow), but there were insufficient amounts of the pigments for identification. Chromatography of the benzene and the ether extracts indicated traces of anthraquinones. Paper chromatography of the ether extract showed the presence of rutin and quercetin.

The considerable amount of brown gum extracted by methanol crystallised on treatment with hot water, to give light yellow needles, m. p. *ca.* 170°, decomp. >189°. Repeated recrystallisation from 50% aqueous ethanol afforded yellow needles of rutin, m. p. and mixed m. p. 195° (decomp.) (Found: C, 52·7; H, 5·1. Calc. for $C_{27}H_{30}O_{16}$: C, 53·0; H, 5·0%), $\lambda_{max.}$ 212, 260, 305, and 362 mμ in EtOH (log ε 4·42, 4·26, 3·95, and 4·24) (cf. ref. [6]).

The glycoside was hydrolysed with 10% hydrochloric acid at 100° for 2 hr. The insoluble aglycone on repeated recrystallisation from 60% acetic acid gave quercetin as stout yellow rods, m. p. and mixed m. p. 316—316·5°. Paper chromatography of the aqueous hydrolysate (ethyl acetate–acetic acid–water, 3 : 1 : 3 v/v, followed by spraying with aniline–trichloroacetic acid) revealed glucose and rhamnose.

Hydrolysis of the rutin mother-liquors with aqueous hydrochloric acid gave a blue-green solution; later there was precipitation of considerable black solid. Similar changes are observed when asperuloside is hydrolysed.

The author is indebted to Professor L. H. Briggs for his continued interest and encouragement, to Mr. T. A. Turney, of this Department, for the collection of bark, and to Dr. R. C. Cooper, Auckland Institute and Museum, for its botanical identification.

University of Auckland, Auckland, New Zealand. [*Received, August 5th*, 1958.]

* Part X, *J.*, 1955, 3298.

[1] Oliver, "The Genus *Coprosma*," Bernice P. Bishop Museum Bull., 1935, p. 132.
[2] Sutherland, *New Zealand J. Sci. Technol.*, 1947, **29**, *B*, 94.
[3] Briggs and Nicholls, *J.*, 1954, 3940.
[4] Trim and Hill, *Biochem. J.*, 1952, **50**, 310.
[5] Briggs and Taylor, *J.*, 1955, 3298.
[6] Geissman, "Modern Methods of Plant Analysis," Springer-Verlag, Berlin, 1955, Vol. III, p. 487.

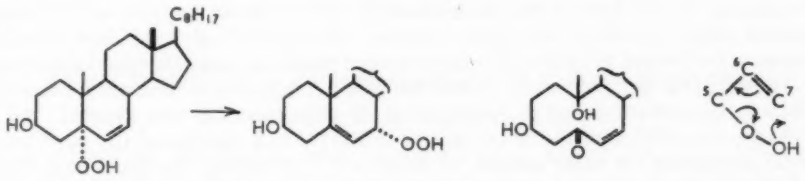
91. *Allylic Rearrangement of an αβ-Unsaturated Hydroperoxide.*

By B. Lythgoe and S. Trippett.

During their studies on the photo-induced reactions of organic compounds and oxygen, Schenck and his co-workers [1] showed that olefins can be converted into αβ-unsaturated hydroperoxides; thus cholesterol gives the 5α-hydroperoxide (I), the hydroperoxyl group becoming attached to one of the termini of the original double bond, whilst the latter migrates to the adjacent position. They also observed [1] that the peroxide (I) in chloroform slowly underwent mutarotation, which, it was suggested, might be due to a rearrangement [2] to the hydroxy-ketone (II) or its internal hemiacetal.

An interest in compounds of type (II) prompted us to examine the rearrangement of the hydroperoxide (I); it was effectively complete at room temperature in chloroform after 12 hr., and the product was then obtained crystalline in very high yield. That the product was a hydroperoxide was shown by its rapid liberation of iodine from potassium iodide in acetic acid; its high negative optical rotation suggested that it contained a 5 : 6-double bond. Controlled catalytic reduction gave in high yield crystalline 7α-hydroxycholesterol; the product is therefore not the hydroxy-ketone (II), but 7α-hydroperoxycholesterol (III).

We believe this rearrangement to be the first example of an allylic rearrangement of an αβ-unsaturated hydroperoxide, and the nature of the change, together with the apparently complete retention of the α-configuration during it, suggests that it takes place through a cyclic 5-membered transition state (IV). This mechanism does not, however, explain the function of the solvent in the reaction. The chloroform used was free from hydrogen chloride, and the reaction did not take place in benzene, methanol, pyridine, or tetrahydrofuran, nor in the latter solvent containing toluene-*p*-sulphonic acid.



(I) (III) (II) (IV)

Professor Schenck has kindly informed us that similar results have also been obtained in his laboratory, and that the allylic rearrangement of (I) has been shown to be an example of a general phenomenon. His results will be published elsewhere.

Experimental.—*7α-Hydroperoxycholesterol.* A suspension of 5α-hydroperoxycholest-6-en-3β-ol [3] (4·6 g.) in chloroform (100 c.c.) was set aside at room temperature for 24 hr. with occasional shaking. Evaporation of the clear solution and crystallisation of the residue from ethyl acetate–light petroleum (b. p. 40—60°) gave *7α-hydroperoxycholesterol* (3·9 g.) as needles, m. p. 154—155° (decomp.), $[\alpha]_D^{17}$ −131° (*c*, 0·8 in pyridine) (Found: C, 77·3; H, 10·9. $C_{27}H_{46}O_3$ requires C, 77·5; H, 11·1%).

7α-Hydroxycholesterol. A solution of 7α-hydroperoxycholesterol (1 g.) in ethanol (60 c.c.) was shaken with palladium–charcoal and hydrogen at room temperature and pressure until 1·0 mol. of hydrogen had been absorbed. Filtration, evaporation of the filtrate, and crystallisation of the residue from aqueous methanol gave 7α-hydroxycholesterol (0·9 g.) as needles, m. p. 183—184°, $[\alpha]_D^{17}$ −86° (*c*, 1·1 in chloroform) (lit. values,[4] m. p. 184—185°, $[\alpha]_D$ −86·4°).

[1] Schenck, *Angew. Chem.*, 1957, **69**, 579.
[2] Hock and Lang, *Ber.*, 1944, **77**, 259.
[3] Schenck, Gollnick, and Neumüller, *Annalen*, 1957, **603**, 46.
[4] Barr, Heilbron, Parry, and Spring, *J.*, 1936, 1437. For proof of the α-configuration see Heymann and Fieser, *Helv. Chim. Acta*, 1952, **35**, 631.

XUM

Acetylation with pyridine–acetic anhydride gave the diacetate, m. p. (from ethanol) 121·5—122·5°, $[\alpha]_D^{17}$ −174° (*c*, 0·9 in chloroform) (lit. values,[4] m. p. 121—122°, $[\alpha]_D$ −174·6°) (Found: C, 76·4; H, 10·2. Calc. for $C_{31}H_{50}O_4$: C, 76·5; H, 10·3%).

THE UNIVERSITY, LEEDS 2.

[*Received, July 24th*, 1958.]

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92 *Thermodynamics of the Hydrogen- and Hydroxy-complexes of Aluminium with Ethylenediaminetetra-acetic Acid.*

By T. RANDALL and L. A. K. STAVELEY.

IN a systematic study of the thermodynamics of the complexes of ethylenediaminetetra-acetic acid (EDTA) with tervalent metals, it was thought worthwhile to extend the measurements with aluminium to give information about the hydrogen complex $Al(H_2O)HY$ present at lower pH values and the hydroxy-complex $Al(OH)Y^{2-}$ present at higher pH values. We have therefore measured ΔH at 20° for the reactions:

$$Al(H_2O)HY \rightleftharpoons Al(H_2O)Y^- + H^+ \quad . . . . . (1)$$

$$Al(H_2O)Y^- \rightleftharpoons Al(OH)Y^{2-} + H^+ \quad . . . . . (2)$$

where Y is the anion of EDTA. There seems little doubt that, in the normal complex, at least one water molecule is closely associated with the aluminium.[1]

The calorimeter used has already been described.[2] The thermal quantities measured were the following. (*a*) The heat change on addition of about a 10% excess of EDTA (approximately in the form of the tetrapotassium salt) to about one litre of a solution of aluminium nitrate (~0·01M) containing sufficient nitric acid to give the final solution of the complex the desired pH and sufficient potassium nitrate to make the final ionic strength 0·1. The pH of the aluminium nitrate solution before complex-formation never exceeded 3. In this way, complications due to hydrolysis of the aluminium ion were avoided. (*b*) The heat change on addition of the same amount of EDTA to a solution of the same volume as in (*a*) containing the same amount of nitric acid but lacking the aluminium nitrate. Sufficient potassium nitrate was again present to make the final ionic strength 0·1. The pH's of the final solutions in (*a*) and (*b*) were measured. Three sets of experiments were carried out, involving different amounts of nitric acid, such that the pH values of the final solution were 3·26, 4·93, and 7·44. Saito and Terrey [1] determined the equilibrium constants at 15° for reactions (1) and (2). Values at 20° (and hence also the derived ΔG values at this temperature) were estimated by using approximate figures for the associated changes in heat content. It was then possible to evaluate the amounts of the complexes $Al(H_2O)HY$, $Al(H_2O)Y^-$, and $Al(OH)Y^{2-}$ present in the final solutions at the different pH values, and so to estimate, not only the heat of formation of the normal complex, but also the changes in heat content for reactions (1) and (2).

The results were as follows: For reaction (1) at 20°, $\Delta H = +3{\cdot}9°$ kcal./mole, whence, since $\Delta G = +3{\cdot}97$ kcal./mole, $\Delta S = \sim 0$ e.u. For reaction (2) at 20°, $\Delta H = +5{\cdot}0$ kcal./mole, whence, since $\Delta G = +8{\cdot}21$ kcal./mole, $\Delta S = -10{\cdot}9$ e.u. The simplest view of the nature of the hydrogen complex is that in the normal complex one $\cdot CH_2 \cdot CO_2^-$ group is free and that the hydrogen complex is formed by the addition of a proton to this group. Reaction (1) above is then essentially the ionization of a carboxylic acid. Usually for the ionization of such an acid ΔH is between 0 and −1 kcal./mole and ΔS is about −20 e.u. That both ΔH and ΔS for reaction (1) are larger than these values may be because the

[1] Saito and Terrey, *J.*, 1956, 4701.
[2] Davies, Singer, and Staveley, *J.*, 1954, 2304; Care and Staveley, *J.*, 1956, 4571.

$\cdot CH_2 \cdot CO_2^-$ group in the normal complex is to some extent prevented by the rest of the complex from interacting as strongly with the water molecules as a simple carboxylate ion does. Another possibility for the hydrogen complex is that the proton is attached to a nitrogen atom. The high positive charge on the nearby aluminium ion could then account for the large drop from, say, the pK_2 of 9·78 for glycine to the value of 2·96 for the aluminium–hydrogen–EDTA complex. The ionization of a proton from a substituted ammonium ion is usually accompanied by a much larger increase in both heat content and entropy than is the ionization of a carboxylic acid, so that this possibility, although perhaps the less likely of the two, is also qualitatively consistent with the observed values of the thermodynamic parameters for the ionization.

For the normal ionization [3] of water at 25°, $\Delta G = 19{\cdot}1$ kcal./mole, $\Delta H = 13{\cdot}5$ kcal./mole and $\Delta S = -18{\cdot}7$ e.u. The much greater acidity of the water molecule in the EDTA complex is hence due partly to a decreased ΔH on ionization and to an increased ΔS. It would naturally be expected that the large charge on the aluminium ion would reduce the energy required for the expulsion of a proton from the adjacent water molecule, while the increased entropy change may arise primarily because the hydroxyl ion produced remains bound in the complex so that it cannot exert the ordering influence which it would have on surrounding water molecules if it were free.

We thank Imperial Chemical Industries Limited for financial assistance.

THE INORGANIC CHEMISTRY LABORATORY, OXFORD. [*Received, July 24th*, 1958.]

[3] Harned and Owen, "The Physical Chemistry of Electrolytic Solutions," 3rd edn., Reinhold Publ. Corp., New York, 1958, p. 667.

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93. *Synthesis of 5-Bromotryptophan and Some Derivatives.*

By D. G. HARVEY.

THE importance of *NN*-diethylbromolysergamide as an active antagonist to serotonin *in vivo* has stimulated interest in bromoindole derivatives. As Shaw and Woolley [1] have recognised the harman type of nucleus in serotonin antagonists it was desirable to prepare the 2-methyl-β-carbolinecarboxylic acid and corresponding carboline base derived from

Compound	Yield, %	Form	M. p.	Formula	Found, % C	Found, % H	Found, % N	Required, % C	Required, % H	Required, % N
5-Bromoindole	75—80	Plates	83°	C_8H_6NBr	49·5	3·2	6·7	48·9	3·1	7·1
5-Bromo-3-dimethylaminomethylindole (5-bromogramine)	65	Leaflets	162	$C_{11}H_{13}N_2Br$	55·5	5·3	10·7	52·1	5·1	11·1
Diethyl (5-bromo-3-indolylmethyl)formamidomalonate	90	Cubes or rhombs	141	$C_{17}H_{19}O_4N_2Br$	49·4	4·7	6·4	49·4	4·6	6·8
5-Bromotryptophan	66	Leaflets	251	$C_{11}H_{11}O_2N_2Br,2H_2O$	42·5	4·9	8·5	41·4	4·7	8·7
8-Bromo-2 : 3 : 4 : 5-tetrahydro-2-methyl-β-carboline-4-carboxylic acid	66	Needles	268	$C_{13}H_{13}O_2N_2Br,2H_2O$	45·4	4·6	7·7	45·2	4·9	7·9
8-Bromo-2-methyl-β-carboline	52	Needles	246	$C_{11}H_9N_2Br$	55·2	3·6	10·5	55·0	3·4	10·7

5-bromotryptophan and acetaldehyde. The syntheses of 5-bromotryptophan, 8-bromo-2 : 3 : 4 : 5-tetrahydro-2-methyl-β-carbolinecarboxylic acid, and 8-bromo-2-methyl-β-carbolin are now reported.

[1] Shaw and Woolley, *J. Biol. Chem.*, 1953, **203**, 69, 979.

XUM

Ethyl 5-bromoindole-2-carboxylate was prepared by cyclisation of ethyl pyruvate *p*-bromophenylhydrazone in polyphosphoric acid (cf. Rydon and Tweddle [2]). The indolecarboxylic acid itself, freed from traces of sulphate, was decarboxylated in good yield to 5-bromoindole by boiling quinoline and copper chromite.

Subsequent steps in the synthesis of the amino-acid and of the carbolines were identical with those used for the synthesis of 5-iodotryptophan; relevant details are summarised in the Table.

Experimental.—All m. p.s are uncorrected.

Ethyl pyruvate p-*bromophenylhydrazone.* This was prepared by esterification of pyruvic acid *p*-bromophenylhydrazone and by the Japp–Klingemann reaction of diazotised *p*-bromoaniline with ethyl α-acetylpropionate. The ester crystallised in very pale brown needles, m. p. 144° (Found: N, 10·0. Calc. for $C_{11}H_{13}O_2N_2Br$: N, 9·8%).

Ethyl 5-bromoindole-2-carboxylate. Ethyl pyruvate *p*-bromophenylhydrazone (35 g.) was well mixed with polyphosphoric acid (65 g. of phosphoric oxide and 40 g. of phosphoric acid). The mixture was warmed to 110—120°; the internal temperature rose sharply to 170° and was kept there for 5 min. It was then cooled to 70°, treated with water, and filtered. The *product* (28 g., 92%) formed needles, m. p. 162°, from ethanol (Found: C, 49·4; H, 3·8; N, 5·3. $C_{11}H_{10}O_2NBr$ requires C, 49·1; H, 3·7; N, 5·2%).

5-Bromoindole-2-carboxylic acid. The ester (28 g.) was hydrolysed [sodium hydroxide (28 g.), ethanol (280 ml.), and water (280 ml.)] for 1·5 hr. under reflux and then kept at room temperature overnight, then acidified. The *acid* formed rhombs (17 g., 68%), m. p. 248°, from alcohol (Found: C, 46·0; H, 2·7; N, 5·8. $C_9H_6O_2NBr$ requires C, 45·0; H, 2·5; N, 5·8%).

I am indebted to Miss L. Butula for valuable assistance.

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LONDON, N.W.1.

[*Received, July* 31*st*, 1958.]

[2] Rydon and Tweddle, *J.* (1955), 3499.
[3] Harvey, *J.*, 1958, 3760.

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94. *Nuclear Magnetic Resonance of* cis-trans-β-*Methylmuconic Acid.*

By J. A. ELVIDGE.

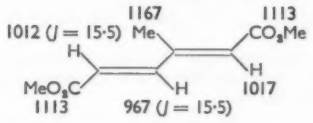
PREVIOUS work [1,2] established that the several routes to β-methylmuconic acid of m. p. *ca.* 170° gave the same material. This, on balance of evidence, was assigned the *cis-trans*-configuration. Reasons were given for rejecting the *cis-cis*-configuration which otherwise was suggested by the preparations from aromatic precursors [1] and particularly from β-methylmuconic anhydride.[2,3] A consequence [2] was that Karrer's first criticism [3] of the Pauling–Zechmeister theory of stereoisomerism in the carotenoids lost its basis. Nevertheless, this criticism was later upheld by the preparation of genuine examples of hindered *cis*-polyenes (*e.g.*, refs. 4, 5). Because of this, Gabers, Eugster, and Karrer wrote: [6] " Eine andere Ausnahme glaubten wir früher in der *cis-cis*-β-methylmuconsäure gefunden zu haben. Diese Substanz wurde dann aber von J. A. Elvidge, R. P. Linstead, and P. Sims als *cis-trans*-Verbindung gedeutet. Die Versuche von Linstead *et al.* sollen überprüft werden."

Reinvestigation of the β-methylmuconic acid in question has now unambiguously confirmed the *cis-trans*-configuration.

[1] Elvidge, Linstead, and Sims, *J.*, 1951, 3386.
[2] *Idem, ibid.*, p. 3398.
[3] Karrer, Schwyzer, and Neuwirth, *Helv. Chim. Acta*, 1948, **31**, 1210.
[4] Gabers, Eugster, and Karrer, *ibid.*, 1952, **35**, 1850.
[5] Oroshnik, Karmas, and Mebane, *J. Amer. Chem. Soc.*, 1952, **74**, 295.
[6] Ref. 4, p. 1858.

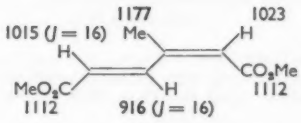
Jackman and Wiley [7] have found that nuclear magnetic resonance spectroscopy readily distinguishes between the *cis*- and *trans*-forms of trisubstituted olefins of the type $RR'C{:}CH{\cdot}CO_2Me$. Further, the method shows with certainty whether such an olefin is a mixture of the two geometrical isomers, provided one of the pure forms is available. Their method has now been extended.

There is no disagreement about an all *trans*-configuration for the high-melting β-methylmuconic acid, m. p. *ca.* 235° (decomp.). This can safely be taken as a reference compound. Its dimethyl ester gave a spectrum in carbon disulphide which showed the expected seven proton resonance lines. There were three singlets at 1167 (C–Me), 1113 (O–Me) and 1017 c./sec. $\left(=C\!<^{H}\right)$ and two doublets with weighted-mean positions at 1012 and 967 c./sec. The large splitting observed for the doublets (J = 15·5 c./sec.) identifies the two hydrogen atoms responsible as those arranged *trans* about an ethylenic link.[8] The interpretation of the resonance spectrum is unique; it is in agreement with the *trans-trans*-configuration and must be as shown in (I).



±1·0 c./sec.

(I)



±2·5 c./sec.

(II)

The results summarised earlier [1,2] showed that the lower-melting β-methylmuconic acid (m. p. *ca.* 170°) had at least one *cis*-arrangement. The possibilities were that it was the *cis-trans*- or less probably the *cis-cis*-isomer. That it might have been a molecular compound of two geometrical forms was not considered. Its dimethyl ester gave a spectrum in carbon disulphide which again showed only three singlets and two doublets. This proves that the compound is a single isomer and not a mixture or molecular compound. The singlet proton resonance lines were at 1177 (C–Me), 1112 (O–Me), and 1023 c./sec. $\left(=C\!<^{H}\right)$. The doublets had weighted-mean positions at 1015 and 916 c./sec. with J = 16 c./sec. so that the two hydrogen atoms responsible are again identified as those *trans* about a double bond. The large drop in weighted-mean frequency for one of the doublets, from 967 in the all-*trans*-isomer to 916 c./sec., indicates that the hydrogen atom responsible is now in a hindered position in the second isomer. Moreover, the C–Me proton resonance, occurring at 10 c./sec. *higher* frequency (1177) than in the all-*trans*-compound (1167 c./sec.) must now be *trans* to methoxycarbonyl, rather than *cis* as in (I).

Again, the interpretation is unique and indicates the *cis-trans*-geometrical form (II) for the lower-melting β-methylmuconate and so for the acid. Karrer's contention that this β-methylmuconic acid, derivable from β-methylmuconic anhydride, has the all-*cis*-configuration [3,4] is therefore incorrect.

The opportunity is taken to correct the ultraviolet absorption data previously given [1] for the two β-methylmuconic acids and ten derivatives. Each of these compounds has a single, rather broad maximum at 264—266 mμ so that the subsidiary inflexions and peaks (on p. 3389, ref. 1) should be deleted. The reason for such mis-readings has been discussed.[9]

[7] Jackman and Wiley, *Proc. Chem. Soc.*, 1958, 196; in last line, 2nd para., for "*cis*" read "*trans*".
[8] Pople, "Applications of Electron and Nuclear Resonance in Chemistry," *Chem. Soc. Special Publ.*, No. 12, 1958, p. 211.
[9] Allan, Jones, and Whiting, *J.*, 1955, 1862.

XUM

Experimental.—trans-trans-β-Methylmuconic acid was prepared from 4-methyl*cyclo*hexanol as before [1] except that the crude dark product was extracted with dry ether in a Soxhlet apparatus. The acid then formed tiny colourless crystals, m. p. 235° (decomp.). This was converted by brief treatment with ethereal diazomethane, filtration, and evaporation into the dimethyl ester which crystallised from light petroleum (b. p. 40—60°) as needles, m. p. 57° (Found: C, 58·7; H, 6·5. Calc. for $C_9H_{12}O_4$: C, 58·7; H, 6·6%).

cis-trans-β-Methylmuconic acid,[1,2] m. p. 171° (decomp.), was similarly esterified to give in near-quantitative yield the dimethyl ester which formed needles, m. p. 38°, from light petroleum (b. p. 40—60°) or carbon tetrachloride at 0° (Found: C, 58·6; H, 6·6%).

The proton magnetic resonance data were obtained with a Varian Associates nuclear magnetic resonance spectrometer with a 40 megacycle oscillator. The spectra were calibrated against tetramethylsilane as an internal reference.[10] Tetramethylsilane at infinite dilution in carbon tetrachloride gives a signal at 1257 cycles per second relative to the aromatic C–H line of external toluene, which is given the arbitrary value of 1000 c./sec.

I am very grateful to Dr. L. M. Jackman of this Department for his help with the nuclear magnetic resonance spectra.

Chemistry Department, Imperial College of Science and Technology,
London, S.W.7. [*Received, September 8th*, 1958.]

[10] Van Dyke Tiers, "Proton Nuclear Spin Resonance Spectroscopy; Reliable Shielding Values by Internal Referencing with Tetramethylsilane," read at 133rd National Meeting of the Amer. Chem. Soc., San Francisco, April 13—18th, 1958; *J. Phys. Chem.*, 1958, **62**, 1151.

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95. *Preparation of Symmetrically Substituted Deoxybenzoins.*

By P. H. Carter, J. Cymerman Craig, (Miss) Ruth E. Lack, and M. Moyle.

The synthesis of deoxybenzoins from phenylacetyl chloride and benzene has been described;[1] however, direct reduction of the readily accessible benzoin provides a more convenient preparation of symmetrically substituted deoxybenzoins. Reduction of benzoin by zinc dust and acetic acid has been reported,[2] and other procedures employed hydrochloric acid and granulated tin [3] (the only detailed instance [4] affording 48·5% of deoxypiperoin), or amalgamated powdered tin [5] (giving 70% of deoxybenzoin, raised to 88% by distillation of the mother-liquors). We record the following observations on this reduction:

Best results were obtained by using powdered tin of 100—200 mesh size. Tin coarser than this left unchanged benzoin, while finer metal tended to conglomerate and give lower yields. The use of amalgamated tin did not enhance yields. A reflux period of 24 hours was optimal. Reduction in the amounts of either tin or acid lowered the yields. Under the conditions defined above, yields of 93·5% of deoxyanisoin, 89% of deoxypiperoin, and 84% of deoxybenzoin were obtained in one step, without the need for distillation of the product.

Experimental.—Deoxyanisoin. Anisoin (52 g., 0·19 mole) and 10N-hydrochloric acid (52 c.c.) were added to powdered tin (40 g., 0·33 mole; 100—200 mesh) and 95% ethanol (60 c.c.), and the mixture was refluxed for 24 hr. The boiling solution was decanted from undissolved tin, cooled to 0°, and filtered. The boiling filtrate was used to wash the tin, and

[1] Allen and Barker, *Org. Synth.*, 1943, Coll. Vol. II, p. 156.
[2] Kohler and Nygaard, *J. Amer. Chem. Soc.*, 1930, **52**, 4133.
[3] Buck and Jenkins, *ibid.*, 1929, **51**, 2163.
[4] Allen and Buck, *ibid.*, 1930, **52**, 310.
[5] Ballard and Dehn, *ibid.*, 1932, **54**, 3970.

the washings were cooled to 0° and filtered. Recrystallisation of the combined solids from 95% ethanol (450 c.c.) gave deoxyanisoin (46 g., 93·5%), m. p. and mixed m. p. 109—110°. A mixed m. p. with anisoin was 92—95°.

Deoxybenzoin. Benzoin (53 g., 0·25 mole), 10N-hydrochloric acid (53 c.c.), tin (53 g., 0·445 mole), and 95% ethanol (50 c.c.) gave deoxybenzoin (84%), m. p. and mixed m. p. 56—58°.

Deoxypiperoin. Piperoin (14·25 g., 0·048 mole), 10N-hydrochloric acid (13 c.c.), tin (10 g., 0·082 mole), and 95% ethanol (30 c.c.) afforded deoxypiperoin (89%), m. p. and mixed m. p. 112—114°. A mixed m. p. with piperoin was 90—95°.

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N.S.W., AUSTRALIA. [*Received, September 15th*, 1958.]

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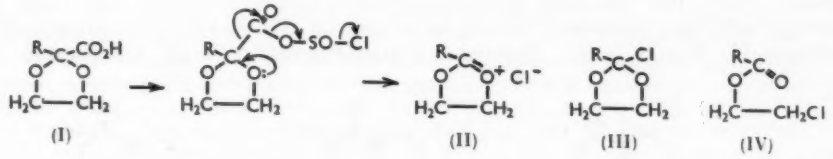
96. *The Action of Thionyl Chloride on 2-Methyl- and 2-Ethyl-1 : 3-dioxolan-2-carboxylic Acid.**

By R. P. A. SNEEDEN.

SCHINZ and VOGEL [1] recorded the isolation of a compound $C_5H_9O_2Cl$ after reaction of thionyl chloride with 2-ethyl-1 : 3-dioxolan-2-carboxylic acid (I; R = Et), and from its conversion by boiling water into propionic acid and its other reactions suggested that it was 2-chloro-2-ethyl-1 : 3-dioxolan (III; R = Et); they comment that its reactivity is between that of an acid chloride and an alkyl halide.



(I) (II) (III) (IV)

Because of the many potential uses of this type of substance an attempt was made to prepare the analogous compound from the 2-methyl-acid (I; R = Me). This gave a chloro-compound, whose homogeneity was established by distillation and a comparison of the infrared spectra of arbitrary fractions: bands at 1740, 1075, 1040, and 660 cm.$^{-1}$ indicated the presence of an ester and a C–Cl group. Consideration of the probable reaction sequence indicates that the initial product would be the oxonium chloride (II). The formation of compound (III; R = Me) (as indicated by Schinz and Vogel's work [1]) would involve formation, without rearrangement, of a C–Cl bond from (II). However, in accordance with the reactions of keten ketals [2] the oxonium ion of (II) should undergo rearrangement to 2-chloroethyl acetate (IV; R = Me). Indeed the reaction product was this compound.

Re-investigation of the action of thionyl chloride on 2-ethyl-1 : 3-dioxolan-2-carboxylic acid (I; R = Et) then showed that the product was the expected 2-chloroethyl propionate (IV; R = Et).

* Submitted in part to the XVIth Internat. Congress Pure Appl. Chem., Paris, 1957.

[1] Schinz and Vogel, *Helv. Chim. Acta*, 1950, **33**, 116.
[2] McElvain and Aldridge, *J. Amer. Chem. Soc.*, 1953, **75**, 3993.

XUM

Experimental.—*2-Methyl-1 : 3-dioxolan-2-carboxylic acid.* The ethylene ketal [3] of ethyl pyruvate (7·65 g.; b. p. 84—89°/17 mm., n_D^{17} 1·4250) was added with cooling to potassium hydroxide (4·05 g.) in water (5·05 c.c.). Concentrated hydrochloric acid (7·0 g.) was added and the product isolated by continuous extraction with ether (15 hr.). Fractional distillation of the dried extract gave *2-methyl-1 : 3-dioxolan-2-carboxylic acid*, b. p. 127—130°/14 mm., n_D^{19} 1·4440 (Found: C, 45·6; H, 6·25. $C_5H_8O_4$ requires C, 45·45; H, 6·1%).

Action of thionyl chloride on the above acid. The acid (12·8 g.) was kept in pure thionyl chloride (7·5 c.c.) overnight. Fractional distillation then gave unchanged thionyl chloride and 2-chloroethyl acetate, b. p. 143°, n_D^{18} 1·4250 (lit., b. p. 143°, n_D^{18} 1·4252). The infrared spectra of this and an authentic specimen were superposable.

2-Ethyl-1 : 3-dioxolan-2-carboxylic acid. The ethylene ketal of ethyl α-oxobutyrate [3] (7·4 g.; b. p. 150—160°/32 mm., n_D^{17} 1·4275) was hydrolysed as described above. The product, on distillation, gave 2-ethyl-1 : 3-dioxolan-2-carboxylic acid, b. p. 160—165°/34 mm., $n_D^{17\cdot5}$ 1·4530.

This acid (1 g.), treated with thionyl chloride as described, gave 2-chloroethyl propionate, b. p. 80—85°/60 mm., n_D^{14} 1·4320 (lit., b. p. 80—85°/60 mm., n_D^{14} 1·4322). The infrared spectra of this and an authentic specimen were superposable.

THE UNIVERSITY, GLASGOW. [*Received, September 19th*, 1958.]

[3] Kuhn, *J. prakt. Chem.*, 1940, **156**, 143.

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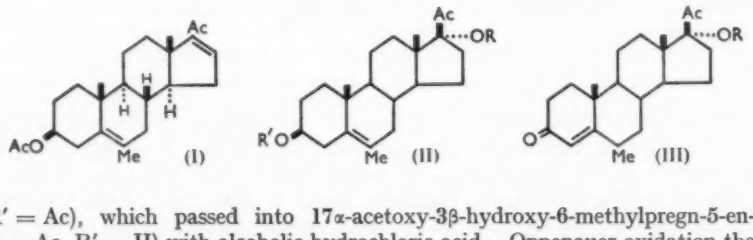
97. *Preparation of 17α-Acetoxy-6α-methylprogesterone.*

By (MISS) S. P. BARTON, B. ELLIS, and V. PETROW.

TREATMENT of 3β-acetoxy-6-methylpregna-5 : 16-dien-20-one [1] (I) with alkaline hydrogen peroxide gave 16α : 17α-epoxy-3β-hydroxy-6-methylpregn-5-en-20-one, converted by hydrogen iodide and subsequent dehalogenation into 3β : 17α-dihydroxy-6-methylpregn-5-en-20-one (II; R = R′ = H). Drastic acetylation [2] furnished the 3β : 17α-diacetate (II;



R = R′ = Ac), which passed into 17α-acetoxy-3β-hydroxy-6-methylpregn-5-en-20-one (II; R = Ac, R′ = H) with alcoholic hydrochloric acid. Oppenauer oxidation then gave 17α-acetoxy-6α-methylprogesterone (III; R = Ac), a highly active progestational agent independently prepared by Babcock *et al.*[3]. Careful alkaline hydrolysis [4] of the monoacetate gave 17α-hydroxy-6α-methylprogesterone (III; R = H). Other 17α-acyl derivatives can be similarly prepared.

Experimental.—Optical rotations were measured in chloroform solutions in a 1-dm. tube. The ultraviolet absorption spectrum (in ethyl alcohol) was kindly determined by Mr. M. T. Davies, B.Sc.

[1] Burn, Ellis, Petrow, (Mrs.) Stuart-Webb, and Williamson, *J.*, 1957, 4092.
[2] Cf. Turner, *J. Amer. Chem. Soc.*, 1953, **75**, 3489.
[3] Babcock, Gutsell, Herr, Hogg, Stuki, Barnes, and Dulin, *J. Amer. Chem. Soc.*, 1958, **80**, 2904; cf. Cooley, Ellis, Kirk, and Petrow, *J.*, 1957, 4112.
[4] Ringold, Löken, Rosenkranz, and Sondheimer, *J. Amer. Chem. Soc.*, 1956, **78**, 816.

16 : 17α-*Epoxy*-3β-*hydroxy*-6-*methylpregn*-5-*en*-20-*one*. 3β-Acetoxy-6-methylpregna-5 : 16-dien-20-one [1] (20 g.) in boiling methanol (250 ml.) was treated with aqueous sodium hydroxide (40%; 40 ml.), followed immediately by hydrogen peroxide (30%; 40 ml.) added dropwise during 5 min. The mixture was refluxed for 20 min. and then poured into water, and the solids were collected and purified from aqueous ethanol. The *epoxide hydrate* formed plates, m. p. 180—182°, $[\alpha]_D^{23}$ −8° (*c* 0·94) (Found: C, 72·8, 72·8; H, 9·4, 9·3. $C_{22}H_{32}O_3,H_2O$ requires C, 72·9; H, 9·45%). The *anhydrous compound* (Found: C, 76·2; H, 9·2. $C_{22}H_{32}O_3$ requires C, 76·7; H, 9·4%) was obtained by heating the hydrate *in vacuo* at 150°. The 3β-*acetate* separated in needles (from acetone–hexane), m. p. 136—137°, $[\alpha]_D^{24}$ −18° (*c* 0·25) (Found: C, 74·1; H, 8·8. $C_{24}H_{34}O_4$ requires C, 74·6; H, 8·8%).

3β : 17α-*Dihydroxy*-6-*methylpregn*-5-*en*-20-*one* (II; R = R′ = H). The 3β-hydroxy-steroid (12 g.) in dioxan (400 ml.) was treated for 30 min. with aqueous hydrogen iodide (55%; 84 ml.). The mixture was poured into water (3 l.), and the precipitate collected and washed until neutral. Its solution in ethanol (500 ml.) was mechanically shaken for 30 min. with Raney nickel (120 g. of sludge), the nickel filtered off and the filtrate taken to dryness under reduced pressure. Trituration of the residue with ether gave a solid which was purified from acetone–hexane. 3β : 17α-*Dihydroxy*-6-*methylpregn*-5-*en*-20-*one hydrate* separated in needles, m. p. 221—222°, $[\alpha]_D^{22}$ −85° (*c* 0·95) (Found: C, 72·8; H, 10·0. $C_{22}H_{34}O_3,H_2O$ requires C, 72·5; H, 10·0%). The *anhydrous compound* (Found: C, 76·1; H, 9·7. $C_{22}H_{34}O_3$ requires C, 76·3; H, 9·9%) was obtained from the hydrate *in vacuo* at 150°.

3β : 17α-*Diacetoxy*-6-*methylpregn*-5-*en*-20-*one* (II; R = R′ = Ac), formed by treating the foregoing compound (5 g.) with acetic anhydride (50 ml.) and toluene-*p*-sulphonic acid (1 g.) for 24 hr. at room temperature, crystallised from aqueous methanol in needles, m. p. 187—188°, $[\alpha]_D^{26}$ −76° (*c* 1·14) (Found: C, 72·4; H, 9·1. $C_{26}H_{38}O_5$ requires C, 72·5; H, 8·9%).

17α-*Acetoxy*-3β-*hydroxy*-6-*methylpregn*-5-*en*-20-*one* (II; R = Ac, R′ = H), formed by heating the diacetate (10 g.) under reflux with methanol (300 ml.) and concentrated hydrochloric acid (2 ml.) for 1½ hr., crystallised from acetone–hexane in needles, m. p. 219—222°, $[\alpha]_D^{23}$ −72° (*c* 0·92) (Found: C, 74·6; H, 9·3. $C_{24}H_{36}O_4$ requires C, 74·2; H, 9·3%).

17α-*Acetoxy*-6α-*methylprogesterone* (III; R = Ac). A solution of the foregoing compound (7·5 g.) in toluene (300 ml.) and *cyclo*hexanone (70 ml.) was distilled until 75 ml. of distillate had collected. After the addition of aluminium *iso*propoxide (3·5 g.) in toluene (100 ml.), the mixture was refluxed for 1 hr., cooled, and treated with excess of aqueous Rochelle salt. The solvents were removed by steam-distillation, and the solid obtained was crystallised from aqueous acetone. 17α-Acetoxy-6α-methylprogesterone formed needles, m. p. 205—208°, $[\alpha]_D^{21}$ +51° (*c* 1·2), $\lambda_{max.}$ 239 mμ (log ε 4·19) (Found: C, 74·3; H, 9·0. Calc. for $C_{24}H_{34}O_4$: C, 74·6; H, 8·9%). Babcock *et al.*[3] give m. p. 205—209°, $[\alpha]_D$ +56°, $\lambda_{max.}$ 240 mμ (log ε 4·20).

17α-*Hydroxy*-6α-*methylprogesterone* (III; R = H). To a refluxing solution of the acetate (3·7 g.) in methanol (100 ml.), there was added, under nitrogen, potassium hydroxide (700 mg.) in methanol (15 ml.) and water (3 ml.), introduced dropwise during 45 min. The mixture was refluxed for a further 2 hr. and then acidified with acetic acid, and water was added to the point of crystallisation. The product was purified from acetone–hexane, giving 17α-hydroxy-6α-methylprogesterone as needles, m. p. 220—223°, $[\alpha]_D^{22}$ +78° (*c* 1·04) (Found: C, 76·7; H, 9·4. Calc. for $C_{22}H_{32}O_3$: C, 76·7; H, 9·4%). The compound occasionally separated in a second form, m. p. *ca.* 264°, which, however, reverted to the lower-melting variety on storage for several days at room temperature. Babcock *et al.*[3] give m. p. 220—223·5°, $[\alpha]_D$ +75°.

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98. 11-*Ethoxy*-1 : 2 : 3 : 4 : 10 : 11-*hexahydrofluoren*-1-*one*. *A Correction.*

F. H. Howell and D. A. H. Taylor.

Some time ago we described the cyclisation of γ-1-(or -3)-indenylbutyronitrile [1] by means of sulphuric acid in ethanol to a compound to which we assigned the structure 11-ethoxy-1 : 2 : 3 : 4 : 10 : 11-hexahydrofluoren-1-one. The evidence for this was the analysis of the compound for carbon and hydrogen, and the fact that it gave 1 : 2 : 3 : 4-tetrahydrofluoren-1-one dinitrophenylhydrazone. We now find that the compound contains nitrogen. The analysis corresponds to that expected for 1 : 2 : 3 : 4 : 10 : 11-*hexahydro*-10-(or -11)-*hydroxy*-1-*iminofluorene*, possible products from the internal attack of the protonated cyano-group on the indenyl double bond, followed by the addition of hydroxyl ion (Found: C, 77·4, 78·1; H, 7·5, 7·8; N, 7·0. $C_{13}H_{15}ON$ requires C, 77·6; H, 7·5; N, 7·0%).

Department of Organic Chemistry, Liverpool University. [*Received, October 27th*, 1958.]

[1] Howell and Taylor, *J.*, 1957, 3011.

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